TENT COOPERATION TRE[illegible]

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 15 February 2000 (15.02.00)	
International application No. PCT/CA99/00529	**Applicant's or agent's file reference** GP/10875.79
International filing date (day/month/year) 04 June 1999 (04.06.99)	**Priority date** (day/month/year) 04 June 1998 (04.06.98)
Applicant SINDERBY, Christer et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

30 December 1999 (30.12.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer S. Mafla
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

15

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
GP/10875.79		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00529	04/06/1999	04/06/1998
International Patent Classification (IPC) or national classification and IPC A61M16/00		
Applicant UNIVERSITE DE MONTREAL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 17 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30/12/1999	04.09.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Valfort, C Telephone No. +49 89 2399 2352

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/00529

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-24 as originally filed

Claims, No.:

1-59 with telefax of 30/12/1999

Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-59.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-59.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No international search report has been established for the amended claims 1 to 59 filed on 30.12.1999, in replacement of unique originally filed claim 1, thus no meaningful examination can be carried out for those amended claims.

CLAIMS

1. A closed loop system for controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical lung ventilator, comprising:

means for measuring (a) the intensity of the diaphragm electromyogram (EMG) for a given Inspiratory volume, (b) the Inspiratory volume for a given EMG intensity, and/or (c) a combination of (a) and (b); and

means for controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical lung ventilator in response to measurement of (a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume, (b) the inspiratory volume for a given EMG intensity, and/or (c) the combination of (a) and (b);

wherein the closed loop system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency such that the neural drive remains stable at a desired target level.

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Dubuc, J.
GOUDREAU GAGE DUBUC &
MARTINEAU WALKER
The Stock Exchange Tower
800 Place Victoria, Suite 3400
Montréal, Québec H4Z 1E9
CANADA

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	23.02.2000
Applicant's or agent's file reference: GP/10875.79	REPLY DUE: **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00529	04/06/1999	04/06/1998

International Patent Classification (IPC) or both national classification and IPC

A61M16/00

Applicant

UNIVERSITE DE MONTREAL et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☐	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☒	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 04/10/2000.

Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer / Examiner Valfort, C Formalities officer (incl. extension of time limits) Moris, A Telephone No. +49 89 2399 8588

Form PCT/IPEA/408 (cover sheet) (January 1994)

WRITTEN OPINION

International application No. PCT/CA99/00529

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-24 as originally filed

Claims, No.:

1-59 with telefax of 30/12/1999

Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire International application,

☒ claims Nos. 1-59,

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

WRITTEN OPINION

International application No. PCT/CA99/00529

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-59 .

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

WRITTEN OPINION
SEPARATE SHEET

International application No. PCT/CA99/00529

Re Item I

Basis of the opinion

(additional observations)

1. The examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT has not been carried out yet.

2. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT).

   If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

Re Item VII

Certain defects in the international application

1. The independent claim should be cast in the two part form according to Rule 6.3.b) PCT.

2. All the claims should contain reference numerals according to Rule 6.2.b) PCT.

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line

IPEA/ _____

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND

Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION

Applicant's or agent's file reference: GP/10875.79

International application No.	International filing date *(day/month/year)*	(Earliest) Priority date *(day/month/year)*
PCT/CA99/00529	04 June 1999 (04/06/99)	04 June 1998 (04/06/98)

Title of invention
PROPORTIONAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL

Box No. II APPLICANT(S)

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country.)*

UNIVERSITÉ DE MONTRÉAL
2900 Boulevard Édouard-Montpetit
Montréal, Québec
Canada, H3C 3J7

Telephone No.: (514) 343-2307
Facsimile No.: (514) 343-2326
Teleprinter No.:

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
CA	CA

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

SINDERBY, Christer
12750, 27th Avenue
Montreal, Quebec
Canada, H1E 1Z9

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
CA	CA

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

BECK, Jennifer
12750, 27th Avenue
Montreal, Quebec
Canada, H1E 1Z9

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
CA	CA

☐ Further applicants are indicated on a continuation sheet.

Sheet No. 2.

International application No.
PCT/CA99/00529

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative

and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.

☐ is hereby appointed and any earlier appointment of (an) agent(s) /common representative is hereby revoked.

☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official The address must include postal code and name of country.)*

DUBUC, Jean H.; LECLERC, Alain M.; PRINCE, Gaëtan; LUPIEN, Marc
GOUDREAU GAGE DUBUC & MARTINEAU WALKER
The Stock Exchange Tower
800 Place Victoria, Suite 3400
Montreal, Quebec, H4Z 1E9, CANADA

Telephone No.: (514) 397-7609

Facsimile No.: (514) 397-4382

Teleprinter No.:

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed.

the description	☒	as originally filed
	☐	as amended under Article 34
the claims	☐	as originally filed
	☐	as amended under Article 19 (together with any accompanying statement)
	☒	as amended under Article 34
the drawings	☒	as originally filed
	☐	as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examing Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH

☒ which is the language in which the international application was filed.
☐ which is the language of a translation furnished for the purposes of international search.
☐ which is the language of publication of the international application.
☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

Sheet No. 3.

International application No.
PCT/CA99/00529

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:			For International Preliminary Examining Authority use only: received	not received
1. translation of international application	:	sheets	☐	☐
2. amendments under Article 34	:	19 sheets	☐	☐
3. copy (or where required, translation) of amendments under Article 19	:	sheets	☐	☐
4. copy (or, where required, translation) of statement under Article 19	:	sheets	☐	☐
5. letter	:	1 sheets	☐	☐
6. other *(specify)*	:	sheets	☐	☐

The demand is also accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ nucleotide and or amino acid sequence listing in computer readable form
6. ☐ other *(specify)*:

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

GOUDREAU GAGE DUBUC & MARTINEAU WALKER

BY: _____

GAÉTAN PRINCE

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):
3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. ☐ The applicant has been informed accordingly.
4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

CHAPTER II

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No.	PCT/CA98/00529
Applicant's or agent's file reference	GP/10875.78

For International Preliminary Examining Authority use only

Date stamp of the IPEA

Applicant
UNIVERSITÉ DE MONTRÉAL et al

Calculation of prescribed fees

1. Preliminary examination fee	2,998.29	P
2. Handling fee *(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)*	289.46	H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	3,287.75	TOTAL

Mode of Payment

- ☐ authorization to charge deposit account with the IPEA (see below)
- ☐ cheque
- ☐ postal money order
- ☒ bank draft
- ☐ cash
- ☐ revenue stamps
- ☐ coupons
- ☐ other *(specify)*:

Deposit Account Authorization *(this mode of payment may not be available at all IPEAs)*

The IPEA/ _____ ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☐ *(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

Deposit Account Number _____ Date *(day/month/year)* _____ Signature _____

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

Receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* GP/10875.79

Box No. I TITLE OF INVENTION

AUTOMATIC ADJUSTMENT OF APPLIED LEVELS OF VENTILATORY SUPPORT AND EXTRINSIC PEEP BY CLOSED-LOOP CONTROL OF NEURO-VENTILATORY EFFICIENCY

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

UNIVERSITÉ DE MONTRÉAL
2900 Boulevard Édouard-Montpetit
Montréal, Québec
Canada, H3C 3J7

☐ This person is also inventor.

Telephone No.
514-343-2307

Facsimile No.
514-343-2326

Teleprinter No.

State *(that is, country)* of nationality: CA

State *(that is, country)* of residence: CA

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SINDERBY, Christer
12750, 27th Avenue
Montreal, Quebec
Canada
H1E 1Z9

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: CA

State *(that is, country)* of residence: CA

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

DUBUC, Jean H.; LECLERC, Alain M.; PRINCE, Gaétan; LUPIEN, Marc
GOUDREAU GAGE DUBUC & MARTINEAU WALKER
The Stock Exchange Tower
800 Place Victoria, Suite 3400
Montreal, Quebec, H4Z 1E9, CANADA

Telephone No.
(514) 397-7609

Facsimile No.
(514) 397-4382

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Sheet No. ...2...

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

BECK, Jennifer;
12750, 27th Avenue
Montreal, Quebec
Canada
H1E 1Z9

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: CA

State *(that is, country)* of residence: CA

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- ☒ AP **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ EA **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ OA **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- ☒ AL Albania .....
- ☒ AM Armenia .....
- ☒ AT Austria .....
- ☒ AU Australia .....
- ☒ AZ Azerbaijan
- ☒ BA Bosnia and Herzegovina .....
- ☒ BB Barbados
- ☒ BG Bulgaria .....
- ☒ BR Brazil .....
- ☒ BY Belarus .....
- ☒ CA Canada
- ☒ CH and LI Switzerland and Liechtenstein
- ☒ CN China .....
- ☒ CU Cuba .....
- ☒ CZ Czech Republic .....
- ☒ DE Germany .....
- ☒ DK Denmark .....
- ☒ EE Estonia .....
- ☒ ES Spain .....
- ☒ FI Finland .....
- ☒ GB United Kingdom
- ☒ GD Grenada
- ☒ GE Georgia .....
- ☒ GH Ghana .....
- ☒ GM Gambia
- ☒ HR Croatia .....
- ☒ HU Hungary .....
- ☒ ID Indonesia
- ☒ IL Israel .....
- ☒ IN India .....
- ☒ IS Iceland
- ☒ JP Japan .....
- ☒ KE Kenya .....
- ☒ KG Kyrgyzstan .....
- ☒ KP Democratic People's Republic of Korea .....
- ☒ KR Republic of Korea .....
- ☒ KZ Kazakhstan .....
- ☒ LC Saint Lucia
- ☒ LK Sri Lanka
- ☒ LR Liberia
- ☒ LS Lesotho .....
- ☒ LT Lithuania
- ☒ LU Luxembourg
- ☒ LV Latvia
- ☒ MD Republic of Moldova .....
- ☒ MG Madagascar .....
- ☒ MK The former Yugoslav Republic of Macedonia .....
- ☒ MN Mongolia
- ☒ MW Malawi .....
- ☒ MX Mexico .....
- ☒ NO Norway
- ☒ NZ New Zealand .....
- ☒ PL Poland .....
- ☒ PT Portugal .....
- ☒ RO Romania
- ☒ RU Russian Federation .....
- ☒ SD Sudan
- ☒ SE Sweden
- ☒ SG Singapore
- ☒ SI Slovenia .....
- ☒ SK Slovakia .....
- ☒ SL Sierra Leone
- ☒ TJ Tajikistan .....
- ☒ TM Turkmenistan .....
- ☒ TR Turkey .....
- ☒ TT Trinidad and Tobago .....
- ☒ UA Ukraine .....
- ☒ UG Uganda .....
- ☒ US United States of America .....
- ☒ UZ Uzbekistan .....
- ☒ VN Viet Nam .....
- ☒ YU Yugoslavia .....
- ☒ ZW Zimbabwe .....

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☒ AE United Arab Emirates .....
- ☒ ZA South Africa .....
- ☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 4 June 1998	2,239,673	CA		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*

ISA/

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*

Date *(day/month/year)* Number Country (or regional Office)

Box No. VIII CHECK LIST: LANGUAGE OF FILING

This international application contains the following number of sheets:

request	:	4
description (excluding sequence listing part)	:	24
claims	:	1
abstract	:	1
drawings	:	10
sequence listing part of description	:	
Total number of sheets	:	40

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as items(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other *(specify)*:

Figure of the drawings which should accompany the abstract: 10

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

GOUDREAU GAGE DUBUC & MARTINEAU WALKER

by: _____

GAÉTAN PRINCE

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA/
6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

This sheet is part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference: GP/10875.79

Applicant: UNIVERSITÉ DE MONTRÉAL

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE ..... 200.00 [T]

2. SEARCH FEE ..... 2,088.00 [S]

International search to be carried out by _____

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the International search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 40 sheets.

first 30 sheets ..... 721.00 [b_1]

10 (remaining sheets) x $17.00 (additional amount) = 170.00 [b_2]

Add amounts entered at b_1 and b_2 and enter total at B .. 891.00 [B]

Designation Fees

The international application contains 77 designations.

10 (number of designation fees payable *(maximum 11)*) x 166.00 (amount of designation fee) = 1,660.00 [D]

Add amounts entered at B and D and enter total at I ..... 2,551.00 [I]

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* ..... [P]

5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P, and enter total in the TOTAL box: 4,839.00 TOTAL

☒ The designation fees are not paid at this time.

MODE OF PAYMENT

- ☐ authorization to charge deposit account (see below)
- ☐ bank draft
- ☐ coupons
- ☐ cheque
- ☐ cash
- ☐ other *(specify)*:
- ☐ postal money order
- ☐ revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ CA

- ☐ is hereby authorized to charge the total fees indicated above to my deposit account.
- ☐ is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.
- ☒ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

27G07	June 4, 1999	
Deposit Account Number	Date *(day/month/year)*	Signature

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Dubuc, J.
GOUDREAU GAGE DUBUC &
MARTINEAU WALKER
The Stock Exchange Tower
800 Place Victoria, Suite 3400
Montréal. Québec H4Z 1E9
CANADA

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	04.09.00
Applicant's or agent's file reference GP/10875.79	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA99/00529	04/06/1999	04/06/1998

Applicant
UNIVERSITE DE MONTREAL et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

RECEIVED
11 SEP 2000
GOU

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Ertl, L Tel.+49 89 2399-7447

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
GP/10875.79		
International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/CA99/00529	04/06/1999	04/06/1998
International Patent Classification (IPC) or national classification and IPC A61M16/00		
Applicant UNIVERSITE DE MONTREAL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 17 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☐ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30/12/1999	04.09.00
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Valfort, C Telephone No. +49 89 2399 2352

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/00529

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-24 as originally filed

Claims, No.:

1-59 with telefax of 30/12/1999

Drawings, sheets:

1/10-10/10 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-59.

because:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA99/00529

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*Indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-59.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/CA99/00529

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No international search report has been established for the amended claims 1 to 59 filed on 30.12.1999, in replacement of unique originally filed claim 1, thus no meaningful examination can be carried out for those amended claims.

CLAIMS

1) A method for substantially removing a common noise signal portion from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre, said method comprising:

a) sensing a first electrical signal of a first polarity through first electrodes located on one side of the centre;

b) sensing a second electrical signal of a second polarity through second electrodes located on the other side of said centre;

c) sensing a third electrical signal through third electrodes located between said first electrodes and said second electrodes;

d) combining the first and second electrical signals into a combination signal; and

e) combining the combination signal and the third electrical signal into an output signal.

2) A method for substantially removing a common noise signal portion as recited in claim 1, wherein:

- said first and second polarities are opposite polarities;

- combining the first and second electrical signals comprises subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion; and

- combining the combination signal with the third electrical signal comprises adding the combination signal and the third electrical

signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss.

3) A method for substantially removing a common noise signal portion as recited in claim 1 or 2, further comprising differentially amplifying said first electrical signal, differentially amplifying said second electrical signal, and differentially amplifying said third electrical signal.

4) A method for substantially removing a common noise signal portion as recited in claim 1, 2 or 3, wherein sensing of said first, second and third electrical signals comprises forming with said first, second and third electrodes a series of electrodes having an axis extending through the centre of the polarity reversal region substantially in the direction of polarity reversal.

5) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3 or 4, further comprising applying said output signal substantially free from said common noise signal portion to a ventilatory assistance system.

6) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3, 4 or 5, wherein sensing of said first, second and third electrical signals comprises sensing first, second and third electromyographic signals, respectively, from at least one muscle of a patient, said at least one muscle constituting the electrical signal source.

7) A device for substantially removing a common noise signal portion from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre, said device comprising:

a) a first input responsive to a first electrical signal having a first polarity sensed through first electrodes located on one side of the centre;

b) a second input responsive to a second electrical signal having a second polarity sensed through second electrodes located on the other side of said centre;

c) a third input responsive to a third electrical signal sensed through third electrodes located between the first electrodes and the second electrodes;

d) means for combining the first and second electrical signals into a combination signal; and

e) means for combining the combination signal and the third electrical signal into an output signal.

8) A device for substantially removing a common noise signal portion as recited in claim 7, wherein:

- said first and second polarities are opposite polarities;

- the first and second electrical signals combining means comprises means for subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion; and

- the means for combining the combination signal with the third electrical signal comprises means for adding the combination

signal and the third electrical signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss.

9) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, further comprising a first differential amplifier for amplifying said first electrical signal, a second differential amplifier for amplifying said second electrical signal, and third differential amplifier for amplifying said third electrical signal.

10) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, wherein said first, second and third electrodes form a series of electrodes having an axis extending through the center of the polarity reversal region substantially in the direction of polarity reversal.

11) A device for substantially removing a common noise signal portion as recited in claim 7, 8 or 9, further comprising a ventilatory assistance system to which is supplied said output signal substantially free from said common noise signal portion.

12) A device for substantially removing a common noise signal portion as recited in claim 7, 8, 9, 10 or 11, further comprising means for extracting from said first, second and third electrical signals, a first, second and third electromyographic signals from at least one muscle of a patient, said at least one muscle constituting said electrical signal source.

13) A neuro-ventilatory efficiency computation method for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system, comprising:

a) receiving a first signal representative of inspiratory effort and having a first amplitude;

b) receiving a second signal representative of a lung volume and having a second amplitude;

c) calculating a relation between said first and second amplitudes at predetermined intervals; and

d) increasing or decreasing the ventilatory assist level depending on whether a present calculated value of said relation is higher or lower than a past calculated value of said relation by an amount exceeding a given threshold.

14) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at predetermined time intervals.

15) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at intervals when one of said first and second amplitudes reaches a predetermined level.

16) A neuro-ventilatory efficiency computation method as in claim 13, 14 or 15, wherein the ventilatory assist level increasing or decreasing comprises increasing the ventilatory assist level when said present calculated value of said relation is higher than said past calculated value of said relation by an amount exceeding the given threshold, and

decreasing the ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold.

17) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15 or 16, wherein receiving the second signal representative of a lung volume comprises receiving a signal representative of a given lung volume.

18) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16 or 17, wherein receiving the first signal representative of inspiratory effort comprises receiving a signal representative of a given level of inspiratory effort.

19) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17 or 18, further comprising generating an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold.

20) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, or 19, comprising manually performing said increasing or decreasing of the ventilatory assist level.

21) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the first signal representative of inspiratory effort as one of the following values: a mean

of said first amplitude, a median of said first amplitude, and a peak of said first amplitude.

22) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the second signal representative of a lung volume as one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude.

23) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22 wherein receiving the first signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient.

24) A neuro-ventilatory efficiency computation device for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system, comprising:

a) a first input for receiving a first signal representative of inspiratory effort and having a first amplitude;

b) a second input for receiving a second signal representative of a lung volume and having a second amplitude;

c) means for calculating a relation between said first and second amplitudes at predetermined intervals; and

d) means for increasing or decreasing the ventilatory assist level depending on whether a present calculated value of said relation is higher or lower than a past calculated value of said relation by an amount exceeding a given threshold.

25) A neuro-ventilatory efficiency computation device as in claim 24, wherein:

the calculating means comprises a divider responsive to the first and second amplitudes for calculating a ratio between said first and second amplitudes at predetermined intervals;

the increasing or decreasing means comprises:

- a comparator responsive to the present calculated value and the past calculated value of said relation for producing a signal representative of a comparison between a present calculated value of said relation and a past calculated value of said relation;
- an adder interposed between the comparator and the ventilatory assistance system for adding a preset increment to or subtracting a preset decrement from said ventilatory assist level when the comparison signal exceeds a given threshold.

26) A neuro-ventilatory efficiency computation device as in claim 24 or 25, wherein said calculating means comprises means for calculating said relation at predetermined time intervals.

27) A neuro-ventilatory efficiency computation device as in claim 24, or 25, wherein said calculating means comprises means for calculating said relation at intervals when one of said first and second amplitudes reach a predetermined level.

28) A neuro-ventilatory efficiency computation device as in any one of claims 25 to 27, wherein said adder comprises means for adding said preset increment to said ventilatory assist level when said present calculated value of said relation is higher than said past calculated value

of said relation by an amount exceeding said given threshold, and means for subtracting said preset decrement from said ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold.

29) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of a lung volume is a signal representative of a given lung volume.

30) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of inspiratory effort is a signal representative of a given level of inspiratory effort.

31) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 30, further comprising an alarm generator to produce an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold.

32) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 31, wherein said adder comprises a manual adjustment system to add said preset increment to or subtracting said preset decrement from said ventilatory assist level.

33) A neuro-ventilatory efficiency computation device as in any one of claims 22 to 32, comprising means for expressing the first signal representative of inspiratory effort by means of one of the following

values: a mean of said first amplitude, a median of said first amplitude, and a peak of said first amplitude.

34) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 32, further comprising means for expressing the second signal representative of a lung volume by means of one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude.

35) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 34, wherein the first signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient.

36) A method for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device in relation to a signal representative of inspiratory effort in view of minimizing the level of pre-inspiratory effort, comprising:

a) receiving a signal representative of inspiratory flow;

b) calculating from said inspiratory flow signal an onset time for inspiration;

c) receiving a signal representative of inspiratory effort having an amplitude;

d) calculating a signal representative of pre-inspiratory effort in response to said onset time and said signal representative of inspiratory effort; and

e) increasing or decreasing the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

37) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 36, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

38) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 37, wherein increasing of decreasing the level of positive end expiratory pressure comprises increasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is higher than said given threshold, and decreasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold.

39) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 38, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume.

40) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises

calculating said signal representative of pre-inspiratory effort at said onset time.

41) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

42) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein:

a) calculating said signal representative of pre-inspiratory effort comprises calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time; and

b) increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit.

43) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 39, wherein increasing or decresing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on both whether said period is higher or lower than the given limit, and whether the amplitude of the signal representative of pre-inspiratory effort is higher or lower than a given threshold.

44) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 43, further comprising generating an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

45) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 44, comprising manually performing the increase or decrease of the level of positive end expiratory pressure.

46) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 45, comprising expressing said signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude.

47) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 46, wherein receiving said signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient.

48) A controller for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device in relation to a signal representative of inspiratory effort in view of minimizing the level of pre-inspiratory effort, comprising:

a) a first input for receiving a signal representative of inspiratory flow having an onset time for inspiration;

b) a second input for receiving a signal representative of inspiratory effort having an amplitude;

c) a computer device responsive to said onset time and said signal representative of inspiratory effort to compute said signal representative of pre-inspiratory effort; and

d) an adder/substractor for adding a preset increment to or subtracting a preset decrement from the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

49) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 48, wherein the adder/subtractor comprises means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

50) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 49, wherein the adder/subtractor comprises means for adding the preset increment to the level of positive end expiratory pressure when the signal representative of pre-inspiratory effort is higher than said given threshold, and means for subtracting the preset decrement from the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold.

51) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 50, wherein adder/subtractor comprises means for adding the preset increment to or subtracting the preset decrement from one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume.

52) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort at said onset time.

53) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

54) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein:

a) said computer device comprises means for calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time; and

b) said adder/subtractor comprises means for adding said preset increment to or for subtracting said preset decrement from the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit.

55) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 54, wherein said adding/subtracting means comprise means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on both whether said period is higher or lower than a given limit, and whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

56) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 55, further comprising an alarm generator to produce an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

57) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 56, wherein said adder comprises a manual adjustment system for adding said preset increment to or subtracting said preset decrement from the level of positive end expiratory pressure.

58) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 57, comprising means for expressing the signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude.

59) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 58, wherein the signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient.

PATENT COOPERATION TREA

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
GOUDREAU GAGE DUBUC &
MARTINEAU WALKER
Attn. Dubuc, J.
The Stock Exchange Tower
P.O.Box 242, Victoria-square
Montréal, Québec H4Z 1E9
CANADA

Applicant's or agent's file reference GP/10875.79	Date of mailing *(day/month/year)* 06/10/1999 FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/CA 99/ 00529	International filing date *(day/month/year)* 04/06/1999
Applicant UNIVERSIT DE MONTR AL et al.	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer Nuria Toribio Gonzalez

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continue)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREA

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
GP/10875.79		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 99/ 00529	04/06/1999	04/06/1998
Applicant		
UNIVERSIT DE MONTR AL et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

[ ] the text is approved as submitted by the applicant.

[X] the text has been established by this Authority to read as follows:

PROPORTIONNAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL

5. With regard to the **abstract**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. 10

[X] as suggested by the applicant.

[ ] None of the figures.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

International Application No
CA 99/00529

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M16/00 A61B5/0488

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	E. AGOSTINI ET AL.: "Electromyography of the diaphragm in man and transdiaphragmatic pressure" JOURNAL OF APPLIED PHYSIOLOGY, vol. 15, 1960, pages 1093-1097, XP002115582 page 1093, left-hand column, line 1 - line 22 ---	1
Y	EP 0 776 671 A (SIEMENS ELEMA AB) 4 June 1997 (1997-06-04) column 2, line 8 - line 41 ---	1
A	US 5 671 752 A (SINDERBY CHRISTER ET AL) 30 September 1997 (1997-09-30) column 10, line 15 - line 18; figure 1 --- -/--	1

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 September 1999	06/10/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Zeinstra, H

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
A	WO 97 22377 A (UNIV MANITOBA ;YOUNES MAGDY (CA)) 26 June 1997 (1997-06-26) page 7, line 4 -page 9, line 28; figure 1	1
A	US 5 353 788 A (MILES LAUGHTON E) 11 October 1994 (1994-10-11)	
P,X	WO 98 48877 A (GRASSINO ALEJANDRO ;SINDERBY CHRISTER (SE); FRIBERG SVEN (SE); LIN) 5 November 1998 (1998-11-05) page 10, line 22 -page 11, line 4; figures 1-5 page 16, line 14 -page 17, line 19 page 19, line 16 -page 22, line 4; figure 10	1

2

information on patent family members

International Application No
/CA 99/00529

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0776671 A	04-06-1997	JP 9173454 A	08-07-1997
		US 5720278 A	24-02-1998
US 5671752 A	30-09-1997	CA 2172329 A	01-10-1996
		US 5820560 A	13-10-1998
WO 9722377 A	26-06-1997	AU 1090897 A	14-07-1997
		CA 2240733 A	26-06-1997
		EP 0871509 A	21-10-1998
		JP 11502755 T	09-03-1999
US 5353788 A	11-10-1994	NONE	
WO 9848877 A	05-11-1998	US 5820560 A	13-10-1998
		AU 3534497 A	24-11-1998

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May 23, 2000

BY TELECOPIER

European Patent Office
International Preliminary Examining Authority
D-80298 Munich
GERMANY

Subject: International application No. PCT/CA99/00529
International filing date: 04/06/99
Applicant: UNIVERSITÉ DE MONTRÉAL et al.
"PROPORTIONAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL"

Dear Sirs:

This is in response to the Written Opinion dated February 23, 2000.

As indicated in Applicant's letter dated December 30, 1999, a new set of fifty-nine (59) claims were filed in the present patent application.

Please find enclosed herewith a version of these fifty-nine (59) claims indicating the passages of the application as filed on which the new claims are based.

Regarding the amendment to the abstract, the wording of the new abstract is supported by the new wording of the claims.

Regarding the requirements as to the casting of the independent claims in the two-part form and to the insertion of reference numerals in the claims, these modifications will be dealt with during the prosecution of the corresponding EPO regional phase.

We are looking forward to hearing from the Examiner in this matter.

Yours very truly,

GOUDREAU GAGE DUBUC

Gaétan Prince

GP/cm
Enclosures

CLAIMS

1) A method for substantially removing a common noise signal portion **(page 17, lines 20-25)** from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre **(page 11, lines 7-16)**, said method comprising:

a) sensing a first electrical signal of a first polarity through first electrodes located on one side of the centre **(page 9, lines 10-13; page 10, lines 25-27; page 11, lines 13-16; Figure 4)**;

b) sensing a second electrical signal of a second polarity through second electrodes located on the other side of said centre **(page 9, lines 10-13; page 10, lines 25-27; page 11, lines 13-16; Figure 4)**;

c) sensing a third electrical signal through third electrodes located between said first electrodes and said second electrodes **(page 13, lines 22-24; page 14, lines 10-12)**;

d) combining the first and second electrical signals into a combination signal **(page 14, lines 5-8; step 504 of Figure 5; Figure 7)**; and

e) combining the combination signal and the third electrical signal into an output signal **(page 14, lines 10-15)**.

2) A method for substantially removing a common noise signal portion as recited in claim 1, wherein:

- said first and second polarities are opposite polarities **(page 11, lines 13-16)**;

- combining the first and second electrical signals comprises subtracting one of the first and second electrical signals from the

other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion **(page 14, lines 5-8; step 504 of Figure 5)**; and
- combining the combination signal with the third electrical signal comprises adding the combination signal and the third electrical signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss **(page 14, lines 10-15)**.

3) A method for substantially removing a common noise signal portion as recited in claim 1 or 2, further comprising differentially amplifying said first electrical signal **(page 9, lines 4-6)**, differentially amplifying said second electrical signal **(page 9, lines 4-6)**, and differentially amplifying said third electrical signal **(page 9, lines 4-6)**.

4) A method for substantially removing a common noise signal portion as recited in claim 1, 2 or 3, wherein sensing of said first, second and third electrical signals comprises forming with said first, second and third electrodes a series of electrodes having an axis extending through the centre of the polarity reversal region substantially in the direction of polarity reversal **(12 of Figures 1, 2 and 3; page 8, lines 1-6; page 11, lines 7-16)**.

5) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3 or 4, further comprising applying said output signal substantially free from said common noise signal portion to a ventilatory assistance system **(page 16, lines 12-25)**.

6) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3, 4 or 5, wherein sensing of said first, second and third electrical signals comprises sensing first, second and third electromyographic signals, respectively, from at least one muscle of a patient, said at least one muscle constituting the electrical signal source **(page 8, lines 1-6 and 27; page 9, lines 10-13)**.

7) A device for substantially removing a common noise signal portion **(page 17, lines 20-25)** from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre **(page 11, lines 7-16)**, said device comprising:

a) a first input responsive to a first electrical signal having a first polarity sensed through first electrodes located on one side of the centre **(page 9, lines 10-13; page 10, lines 25-27; page 11, lines 13-16; Figure 4)**;

b) a second input responsive to a second electrical signal having a second polarity sensed through second electrodes located on the other side of said centre **(page 9, lines 10-13; page 10, lines 25-27; page 11, lines 13-16; Figure 4)**;

c) a third input responsive to a third electrical signal sensed through third electrodes located between the first electrodes and the second electrodes **(page 13, lines 22-24; page 14, lines 10-12)**;

d) means for combining the first and second electrical signals into a combination signal **(page 14, lines 5-8; step 504 of Figure 5; Figure 7)**; and

e) means for combining the combination signal and the third electrical signal into an output signal **(page 14, lines 10-15)**.

8) A device for substantially removing a common noise signal portion as recited in claim 7, wherein:

- said first and second polarities are opposite polarities **(page 11, lines 13-16)**;

- the first and second electrical signals combining means comprises means for subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion **(page 14, lines 5-8; step 504 of Figure 5)**; and

- the means for combining the combination signal with the third electrical signal comprises means for adding the combination signal and the third electrical signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss **(page 14, lines 10-15)**.

9) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, further comprising a first differential amplifier for amplifying said first electrical signal **(page 9, line 4-6; 16 of Figure 1)**, a second differential amplifier for amplifying said second electrical signal **(page 9, line 4-6; 16 of Figure 1)**, and third differential amplifier for amplifying said third electrical signal **(page 9, line 4-6; 16 of Figure 1)**.

10) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, wherein said first, second and third electrodes form a series of electrodes having an axis extending through the center of the polarity reversal region substantially in the direction of polarity

reversal **(12 of Figures 1, 2 and 3; page 8, lines 1-6; page 11, lines 7-16)**.

11) A device for substantially removing a common noise signal portion as recited in claim 7, 8 or 9, further comprising a ventilatory assistance system to which is supplied said output signal substantially free from said common noise signal portion **(page 16, lines 12-25)**.

12) A device for substantially removing a common noise signal portion as recited in claim 7, 8, 9, 10 or 11, further comprising means for extracting from said first, second and third electrical signals, a first, second and third electromyographic signals from at least one muscle of a patient, said at least one muscle constituting said electrical signal source **(page 8, lines 1-6 and 27; page 9, lines 10-13)**.

13) A neuro-ventilatory efficiency computation method **(page 19, lines 24-27)** for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system **(page 21, lines 5-17)**, comprising:

a) receiving a first signal representative of inspiratory effort and having a first amplitude **(page 19, lines 25-27; signal 508 in Figure 10)**;

b) receiving a second signal representative of a lung volume and having a second amplitude **(page 19, lines 24-27; see also the "given inspiratory lung volume" signal of Figure 10)**;

c) calculating a relation between said first and second amplitudes at predetermined intervals **(page 19, line 27 and page 20, line 1; page 20, lines 19-22; page 20, lines 26 and 27; and block 602 of Figure 10)**; and

d) increasing **(page 20, lines 3-10; block 606 of Figure 10)** or decreasing **(page 20, lines 12-18; block 608 of Figure 10)** the ventilatory assist level depending on whether a present calculated value of said relation is higher **(page 20, lines 3-7; block 603 of Figure 10)** or lower **(page 20, lines 12-15; block 607 of Figure 10)** than a past calculated value of said relation by an amount exceeding a given threshold.

14) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at predetermined time intervals **(page 18, line 6 to page 19, line 17)**.

15) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at intervals when one of said first and second amplitudes reaches a predetermined level **(page 23, lines 9-23)**.

16) A neuro-ventilatory efficiency computation method as in claim 13, 14 or 15, wherein the ventilatory assist level increasing or decreasing comprises increasing the ventilatory assist level when said present calculated value of said relation is higher than said past calculated value of said relation by an amount exceeding the given threshold **(page 20, lines 3-10)**, and decreasing the ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold **(page 20, lines 12-22)**.

17) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15 or 16, wherein receiving the second signal representative of a lung volume comprises receiving a signal representative of a given lung volume **(page 19, lines 19-21 and 26-27; see "given inspiratory lung volume" signal supplied to block 601 of Figure 10)**.

18) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16 or 17, wherein receiving the first signal representative of inspiratory effort comprises receiving a signal representative of a given level of inspiratory effort **(page 19, lines 21-22)**.

19) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17 or 18, further comprising generating an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold **(page 20, lines 2-24)**.

20) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, or 19, comprising manually performing said increasing or decreasing of the ventilatory assist level **(page 20, lines 22-24; page 21, lines 2-4)**.

21) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the first signal representative of inspiratory effort as one of the following values: a mean of said first amplitude, a median of said first amplitude, and a peak of said first amplitude **(page 20, lines 1-4)**.

22) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the second signal representative of a lung volume as one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude **(page 19, lines 21-22; and page 20, lines 1-4)**.

23) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22 wherein receiving the first signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient **(page 19, lines 25-27; and signal 608 of Figure 10)**.

24) A neuro-ventilatory efficiency computation device **(page 19, lines 24-27)** for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system **(page 21, lines 5-17)**, comprising:

a) a first input for receiving a first signal representative of inspiratory effort and having a first amplitude **(page 19, lines 25-27; signal 508 in Figure 10)**;

b) a second input for receiving a second signal representative of a lung volume and having a second amplitude **(page 19, lines 24-27; see also the "given inspiratory lung volume" signal of Figure 10)**;

c) means for calculating a relation between said first and second amplitudes at predetermined intervals **(page 19, line 27 and page 20, line 1; page 20, lines 26 and 27; and block 602 of Figure 10)**; and

d) means for increasing **(page 20, lines 3-10; block 606 of Figure 10)** or decreasing **(page 20, lines 12-18; block 608 of Figure 10)**

the ventilatory assist level depending on whether a present calculated value of said relation is higher **(page 20, lines 3-7; block 603 of Figure 10)** or lower **(page 20, lines 12-15; block 607 of Figure 10)** than a past calculated value of said relation by an amount exceeding a given threshold.

25) A neuro-ventilatory efficiency computation device as in claim 24, wherein:

the calculating means comprises a divider responsive to the first and second amplitudes for calculating a ratio between said first and second amplitudes at predetermined intervals **(page 18, line 6 to page 19, line 17)**;

the increasing or decreasing means comprises:

- a comparator responsive to the present calculated value and the past calculated value of said relation for producing a signal representative of a comparison between a present calculated value of said relation and a past calculated value of said relation **(page 20, lines 2-22)**;

- an adder interposed between the comparator and the ventilatory assistance system for adding a preset increment to or subtracting a preset decrement from said ventilatory assist level when the comparison signal exceeds a given threshold **(page 20, lines 2-22)**.

26) A neuro-ventilatory efficiency computation device as in claim 24 or 25, wherein said calculating means comprises means for calculating said relation at predetermined time intervals **(page 18, line 6 to page 19, line 17)**.

27) A neuro-ventilatory efficiency computation device as in claim 24, or 25, wherein said calculating means comprises means for calculating said relation at intervals when one of said first and second amplitudes reach a predetermined level **(page 23, lines 9-23)**.

28) A neuro-ventilatory efficiency computation device as in any one of claims 25 to 27, wherein said adder comprises means for adding said preset increment to said ventilatory assist level when said present calculated value of said relation is higher than said past calculated value of said relation by an amount exceeding said given threshold **(page 20, lines 2-22)**, and means for subtracting said preset decrement from said ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold **(page 20, lines 2-22)**.

29) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of a lung volume is a signal representative of a given lung volume **(page 19, lines 19-21 and 26-27; see "given inspiratory lung volume" signal supplied to block 601 of Figure 10)**.

30) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of inspiratory effort is a signal representative of a given level of inspiratory effort **(page 19, lines 21-22)**.

31) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 30, further comprising an alarm generator to produce an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold **(page 20, lines 2-24)**.

32) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 31, wherein said adder comprises a manual adjustment system to add said preset increment to or subtracting said preset decrement from said ventilatory assist level **(page 20, lines 22-24; page 21, lines 2-4)**.

33) A neuro-ventilatory efficiency computation device as in any one of claims 22 to 32, comprising means for expressing the first signal representative of inspiratory effort by means of one of the following values: a mean of said first amplitude, a median of said first amplitude, and a peak of said first amplitude **(page 20, lines 1-4)**.

34) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 32, further comprising means for expressing the second signal representative of a lung volume by means of one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude **(page 19, lines 21-22; and page 20, lines 1-4)**.

35) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 34, wherein the first signal representative of inspiratory effort

is an electromyographic signal from at least one muscle of a patient **(page 19, lines 25-27; and signal 508 of Figure 10)**.

36) A method for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device **(page 3, line 24 to page 4, line 8; page 21, line 21 to page 24, line 3)** in relation to a signal representative of inspiratory effort **(page 22, lines 20-22; see also signal 508 in Figure 11)** in view of minimizing the level of pre-inspiratory effort **(page 4, lines 2-4)**, comprising:

a) receiving a signal representative of inspiratory flow **(page 22 line 24 to page 23, line 2; see signal 703 in Figure 11)** ;

b) calculating from said inspiratory flow signal an onset time for inspiration **(page 23, lines 3-7; block 704 of Figure 11)**;

c) receiving a signal representative of inspiratory effort having an amplitude **(page 22, lines 20-22; signal 508 in Figure 11)**;

d) calculating a signal representative of pre-inspiratory effort in response to said onset time and said signal representative of inspiratory effort **(page 23, lines 9-13; blocks 713 and 714 in Figure 11)**; and

e) increasing **(page 23, lines 9-15; blocks 715, 716 and 708 of Figure 11)** or decreasing **(page 23, lines 17-23; blocks 719, 720 and 711)** the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

37) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 36, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure

depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold **(page 23, lines 9-23; blocks 715-716-708 and 719-720-711 of Figure 11)**.

38) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 37, wherein increasing of decreasing the level of positive end expiratory pressure comprises increasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is higher than said given threshold **(page 23, lines 9-15; blocks 715-716-708 of Figure 11)**, and decreasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold **(page 23, lines 17-23; blocks 719-720-711 of Figure 11)**.

39) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 38, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume **(page 24, lines 4-7)**.

40) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises calculating said signal representative of pre-inspiratory effort at said onset time **(page 23, lines 9-11)**.

41) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time **(page 22, lines 11-15)**.

42) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein:

a) calculating said signal representative of pre-inspiratory effort comprises calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time **(page 22, lines 11-15; page 23, lines 3-7; block 704 of Figure 11)**; and

b) increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit **(page 23, lines 25-27)**.

43) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 39, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on both whether said period is higher or lower than the given limit, and whether the amplitude of the signal representative of pre-inspiratory effort is higher or lower than a given threshold **(page 23, lines**

9-27; blocks 715-716-708 of Figure 11; and blocks 719-720-711 of Figure 11).

44) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 43, further comprising generating an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold **(page 23, lines 9-23; block 716 and 720 of Figure 11).**

45) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 44, comprising manually performing the increase or decrease of the level of positive end expiratory pressure **(page 23, lines 15 and 23).**

46) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 45, comprising expressing said signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude **(block 714 of Figure 11).**

47) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 46, wherein receiving said signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient **(page 22, lines 20-22; signal 508 of Figure 11).**

48) A controller for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device **(page 3, line**

24 to page 4, line 8; page 21, line 21 to page 24, line 3) in relation to a signal representative of inspiratory effort **(page 22, lines 20-22; see also signal 508 of Figure 11)** in view of minimizing the level of pre-inspiratory effort **(page 4, line 2-4)**, comprising:

a) a first input for receiving a signal representative of inspiratory flow having an onset time for inspiration **(page 22, line 24 to page 23, line 2; see signal 703 of Figure 11)**;

b) a second input for receiving a signal representative of inspiratory effort having an amplitude **(page 22, lines 20-22; signal 508 of Figure 11)**;

c) a computer device responsive to said onset time and said signal representative of inspiratory effort to compute said signal representative of pre-inspiratory effort **(page 23, lines 9-13; blocks 713 and 714 of Figure 11)**; and

d) an adder/substractor for adding a preset increment to **(page 23, lines 9-15; blocks 715-716-708 of Figure 11)** or subtracting a preset decrement from **(page 23, lines 17-23; blocks 719-720-711 of Figure 11)** the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort.

49) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 48, wherein the adder/subtractor comprises means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold **(page 23, lines 9-23; blocks 715-716-708 of Figure 11; and blocks 719-720-711 of Figure 11)**.

50) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 49, wherein the adder/subtractor comprises means for adding the preset increment to the level of positive end expiratory pressure when the signal representative of pre-inspiratory effort is higher than said given threshold **(page 23, lines 9-15; blocks 715-716-708 of Figure 11)**, and means for subtracting the preset decrement from the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold **(page 23, lines 17-23; blocks 719-720-711of Figure 11)**.

51) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 50, wherein adder/subtractor comprises means for adding the preset increment to or subtracting the preset decrement from one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume **(page 24, lines 4-7)**.

52) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort at said onset time **(page 23, lines 9-11)**.

53) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort during a period between the time

when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

54) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein:

a) said computer device comprises means for calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time **(page 22, lines 11-15; page 23, lines 3-7; and block 704 of Figure 11)**; and

b) said adder/subtractor comprises means for adding said preset increment to or for subtracting said preset decrement from the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit **(page 23, lines 25-27)**.

55) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 54, wherein said adding/subtracting means comprise means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on both whether said period is higher or lower than a given limit, and whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold **(page 23, lines 9-27; blocks 715-716-708 of Figure 11; and blocks 719-720-711 of Figure 11)**.

56) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 55, further

comprising an alarm generator to produce an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold **(page 23, lines 9-23; blocks 716 and 720 of Figure 11)**.

57) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 56, wherein said adder comprises a manual adjustment system for adding said preset increment to or subtracting said preset decrement from the level of positive end expiratory pressure **(page 23, lines 15 and 23)**.

58) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 57, comprising means for expressing the signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude **(block 714 of Figure 11)**.

59) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 58, wherein the signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient **(page 22, lines 20-22; signal 508 of Figure 11)**.

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Dear Sir/Madam:

Please find enclosed herewith an amendment under Article 34.

This amendment includes new pages 25 to 41 including a new set of 59 claims. This new set of claims replaces the originally filed single claim 1. New claim 13 is an amended version of original single claim 1.

A new page 42 is also attached and contains a new abstract better reflecting the subject matter of the newly submitted set of claims.

We are looking forward to receiving a written opinion in due course.

Yours very truly,

Goudreau Gage Dubuc
& Martineau Walker

Gaétan Prince

GP/CMB/mt
Encl.

CLAIMS

1) A method for substantially removing a common noise signal portion from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre, said method comprising:

a) sensing a first electrical signal of a first polarity through first electrodes located on one side of the centre;

b) sensing a second electrical signal of a second polarity through second electrodes located on the other side of said centre;

c) sensing a third electrical signal through third electrodes located between said first electrodes and said second electrodes;

d) combining the first and second electrical signals into a combination signal; and

e) combining the combination signal and the third electrical signal into an output signal.

2) A method for substantially removing a common noise signal portion as recited in claim 1, wherein:

- said first and second polarities are opposite polarities;

- combining the first and second electrical signals comprises subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion; and

- combining the combination signal with the third electrical signal comprises adding the combination signal and the third electrical

signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss.

3) A method for substantially removing a common noise signal portion as recited in claim 1 or 2, further comprising differentially amplifying said first electrical signal, differentially amplifying said second electrical signal, and differentially amplifying said third electrical signal.

4) A method for substantially removing a common noise signal portion as recited in claim 1, 2 or 3, wherein sensing of said first, second and third electrical signals comprises forming with said first, second and third electrodes a series of electrodes having an axis extending through the centre of the polarity reversal region substantially in the direction of polarity reversal.

5) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3 or 4, further comprising applying said output signal substantially free from said common noise signal portion to a ventilatory assistance system.

6) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3, 4 or 5, wherein sensing of said first, second and third electrical signals comprises sensing first, second and third electromyographic signals, respectively, from at least one muscle of a patient, said at least one muscle constituting the electrical signal source.

7) A device for substantially removing a common noise signal portion from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre, said device comprising:

a) a first input responsive to a first electrical signal having a first polarity sensed through first electrodes located on one side of the centre;

b) a second input responsive to a second electrical signal having a second polarity sensed through second electrodes located on the other side of said centre;

c) a third input responsive to a third electrical signal sensed through third electrodes located between the first electrodes and the second electrodes;

d) means for combining the first and second electrical signals into a combination signal; and

e) means for combining the combination signal and the third electrical signal into an output signal.

8) A device for substantially removing a common noise signal portion as recited in claim 7, wherein:

- said first and second polarities are opposite polarities;

- the first and second electrical signals combining means comprises means for subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion; and

- the means for combining the combination signal with the third electrical signal comprises means for adding the combination

signal and the third electrical signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss.

9) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, further comprising a first differential amplifier for amplifying said first electrical signal, a second differential amplifier for amplifying said second electrical signal, and third differential amplifier for amplifying said third electrical signal.

10) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, wherein said first, second and third electrodes form a series of electrodes having an axis extending through the center of the polarity reversal region substantially in the direction of polarity reversal.

11) A device for substantially removing a common noise signal portion as recited in claim 7, 8 or 9, further comprising a ventilatory assistance system to which is supplied said output signal substantially free from said common noise signal portion.

12) A device for substantially removing a common noise signal portion as recited in claim 7, 8, 9, 10 or 11, further comprising means for extracting from said first, second and third electrical signals, a first, second and third electromyographic signals from at least one muscle of a patient, said at least one muscle constituting said electrical signal source.

13) A neuro-ventilatory efficiency computation method for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system, comprising:

a) receiving a first signal representative of inspiratory effort and having a first amplitude;

b) receiving a second signal representative of a lung volume and having a second amplitude;

c) calculating a relation between said first and second amplitudes at predetermined intervals; and

d) increasing or decreasing the ventilatory assist level depending on whether a present calculated value of said relation is higher or lower than a past calculated value of said relation by an amount exceeding a given threshold.

14) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at predetermined time intervals.

15) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at intervals when one of said first and second amplitudes reaches a predetermined level.

16) A neuro-ventilatory efficiency computation method as in claim 13, 14 or 15, wherein the ventilatory assist level increasing or decreasing comprises increasing the ventilatory assist level when said present calculated value of said relation is higher than said past calculated value of said relation by an amount exceeding the given threshold, and

decreasing the ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold.

17) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15 or 16, wherein receiving the second signal representative of a lung volume comprises receiving a signal representative of a given lung volume.

18) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16 or 17, wherein receiving the first signal representative of inspiratory effort comprises receiving a signal representative of a given level of inspiratory effort.

19) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17 or 18, further comprising generating an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold.

20) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, or 19, comprising manually performing said increasing or decreasing of the ventilatory assist level.

21) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the first signal representative of inspiratory effort as one of the following values: a mean

of said first amplitude, a median of said first amplitude, and a peak of said first amplitude.

22) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the second signal representative of a lung volume as one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude.

23) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22 wherein receiving the first signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient.

24) A neuro-ventilatory efficiency computation device for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system, comprising:

a) a first input for receiving a first signal representative of inspiratory effort and having a first amplitude;

b) a second input for receiving a second signal representative of a lung volume and having a second amplitude;

c) means for calculating a relation between said first and second amplitudes at predetermined intervals; and

d) means for increasing or decreasing the ventilatory assist level depending on whether a present calculated value of said relation is higher or lower than a past calculated value of said relation by an amount exceeding a given threshold.

25) A neuro-ventilatory efficiency computation device as in claim 24, wherein:

the calculating means comprises a divider responsive to the first and second amplitudes for calculating a ratio between said first and second amplitudes at predetermined intervals;

the increasing or decreasing means comprises:

- a comparator responsive to the present calculated value and the past calculated value of said relation for producing a signal representative of a comparison between a present calculated value of said relation and a past calculated value of said relation;
- an adder interposed between the comparator and the ventilatory assistance system for adding a preset increment to or subtracting a preset decrement from said ventilatory assist level when the comparison signal exceeds a given threshold.

26) A neuro-ventilatory efficiency computation device as in claim 24 or 25, wherein said calculating means comprises means for calculating said relation at predetermined time intervals.

27) A neuro-ventilatory efficiency computation device as in claim 24, or 25, wherein said calculating means comprises means for calculating said relation at intervals when one of said first and second amplitudes reach a predetermined level.

28) A neuro-ventilatory efficiency computation device as in any one of claims 25 to 27, wherein said adder comprises means for adding said preset increment to said ventilatory assist level when said present calculated value of said relation is higher than said past calculated value

of said relation by an amount exceeding said given threshold, and means for subtracting said preset decrement from said ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold.

29) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of a lung volume is a signal representative of a given lung volume.

30) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of inspiratory effort is a signal representative of a given level of inspiratory effort.

31) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 30, further comprising an alarm generator to produce an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold.

32) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 31, wherein said adder comprises a manual adjustment system to add said preset increment to or subtracting said preset decrement from said ventilatory assist level.

33) A neuro-ventilatory efficiency computation device as in any one of claims 22 to 32, comprising means for expressing the first signal representative of inspiratory effort by means of one of the following

values: a mean of said first amplitude, a median of said first amplitude, and a peak of said first amplitude.

34) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 32, further comprising means for expressing the second signal representative of a lung volume by means of one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude.

35) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 34, wherein the first signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient.

36) A method for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device in relation to a signal representative of inspiratory effort in view of minimizing the level of pre-inspiratory effort, comprising:

a) receiving a signal representative of inspiratory flow;

b) calculating from said inspiratory flow signal an onset time for inspiration;

c) receiving a signal representative of inspiratory effort having an amplitude;

d) calculating a signal representative of pre-inspiratory effort in response to said onset time and said signal representative of inspiratory effort; and

e) increasing or decreasing the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

37) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 36, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

38) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 37, wherein increasing of decreasing the level of positive end expiratory pressure comprises increasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is higher than said given threshold, and decreasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold.

39) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 38, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume.

40) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises

calculating said signal representative of pre-inspiratory effort at said onset time.

41) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

42) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein:

a) calculating said signal representative of pre-inspiratory effort comprises calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time; and

b) increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit.

43) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 39, wherein increasing or decresing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on both whether said period is higher or lower than the given limit, and whether the amplitude of the signal representative of pre-inspiratory effort is higher or lower than a given threshold.

44) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 43, further comprising generating an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

45) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 44, comprising manually performing the increase or decrease of the level of positive end expiratory pressure.

46) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 45, comprising expressing said signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude.

47) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 46, wherein receiving said signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient.

48) A controller for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device in relation to a signal representative of inspiratory effort in view of minimizing the level of pre-inspiratory effort, comprising:

a) a first input for receiving a signal representative of inspiratory flow having an onset time for inspiration;

b) a second input for receiving a signal representative of inspiratory effort having an amplitude;

c) a computer device responsive to said onset time and said signal representative of inspiratory effort to compute said signal representative of pre-inspiratory effort; and

d) an adder/substractor for adding a preset increment to or subtracting a preset decrement from the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

49) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 48, wherein the adder/subtractor comprises means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

50) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 49, wherein the adder/subtractor comprises means for adding the preset increment to the level of positive end expiratory pressure when the signal representative of pre-inspiratory effort is higher than said given threshold, and means for subtracting the preset decrement from the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold.

51) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 50, wherein adder/subtractor comprises means for adding the preset increment to or subtracting the preset decrement from one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume.

52) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort at said onset time.

53) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

54) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein:

a) said computer device comprises means for calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time; and

b) said adder/subtractor comprises means for adding said preset increment to or for subtracting said preset decrement from the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit.

55) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 54, wherein said adding/subtracting means comprise means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on both whether said period is higher or lower than a given limit, and whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

56) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 55, further comprising an alarm generator to produce an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

57) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 56, wherein said adder comprises a manual adjustment system for adding said preset increment to or subtracting said preset decrement from the level of positive end expiratory pressure.

58) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 57, comprising means for expressing the signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude.

59) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 58, wherein the signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient.

ABSTRACT OF THE DISCLOSURE

A closed loop system uses a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume; b) the inspiratory volume for a given EMG intensity; or c) a combination of a) and b); in view of controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical (lung) ventilator. The closed loop ventilator system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency such that the neural drive remains stable at a desired target level. An alarm can also be used to detect changes in neuroventilatory efficiency in view of performing manual adjustments. This invention also includes a detection and adjustment system for a) determination of pre-inspiratory effort amplitude, and b) determination of pre-inspiratroy effort duration. This system can be used to monitor and/or manually and/or automatically adjust externally applied pressure flow and/or volume in order to determine and control the level of pre-inspiratory effort and/or duration. Finally, the invention describes a system for removing a common noise portion from an electrical signal by detecting, with multiple pairs of electrodes, first, second and third electrical signals from an electrical signal source. The first and second signals being detected from electrode pairs on opposites sides of a polarity reversal center of the electrical signal source, and the third signal being detected from an electrode pair between the first and second pairs. The system then subtracts the second signal from the first signal, and adds the third signal to obtain a substantially noise free signal and thereby substantially prevent signal loss.

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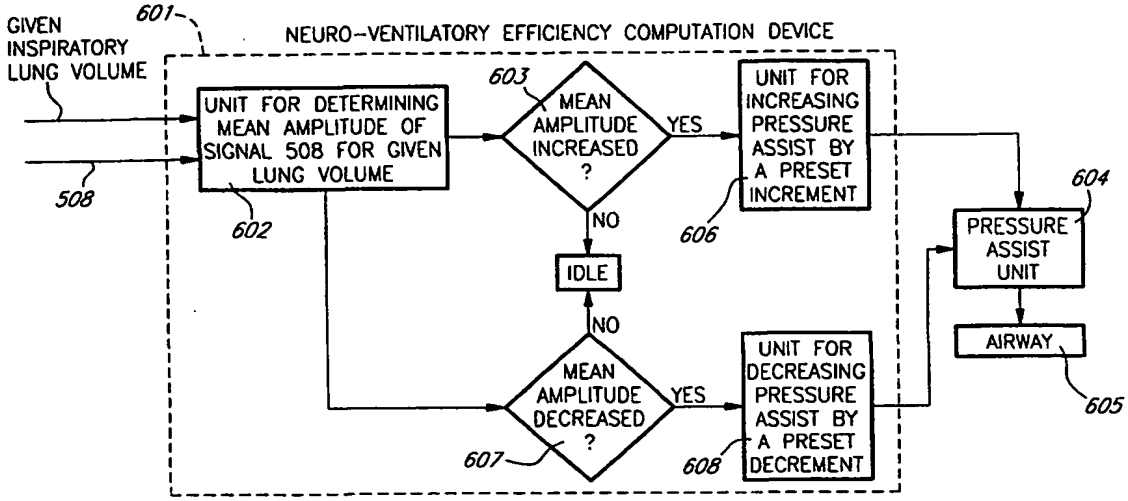

(57) Abstract

A closed loop system uses (a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume; (b) the inspiratory volume for a given EMG intensity; or (c) a combination of (a) and (b); in view of controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical (lung) ventilator. The closed loop ventilator system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro–ventilatory efficiency such that the neural drive remains stable at a desired target level. An alarm can also be used to detect changes in neuroventilatory efficiency in view of performing manual adjustments.

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PROPORTIONAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL

BACKGROUND OF THE INVENTION

1. Field of the invention:

The present invention relates to a system using the intensity of the diaphragm electromyogram (EMG) at a given lung volume or the lung volume at a given EMG intensity to automatically or manually adjust the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency.

The present invention also relates to a system responsive to the intensity of the diaphragm electromyogram (EMG) measured immediately before the onset of inspiratory flow to automatically or manually control and maintain an optimum level of extrinsic positive end expiratory pressure (PEEP) applied to a patient, and to automatically or manually control a duration from the onset of EMG to onset of respiratory flow.

2. Brief description of the prior art:

Prior art algorithms used to create closed-loop ventilator systems are based on variables such as tidal volume, respiratory rate,

inspiratory flow, end-tidal carbon dioxide levels and/or rate of rise in pressure. However, none of these parameters can provide a reliable measure of the respiratory neural drive because they are affected by changes in neuro-mechanical or neuro-ventilatory efficiency.

Neuro-ventilatory efficiency is a term used to express the amount of neural drive (breathing effort) needed to obtain a given tidal lung volume. In brief, neural drive is converted into mechanical tension, a process which is influenced by the muscle length, temperature, electrolyte imbalance, etc. The role of inspiratory flow in the link between neural drive and mechanical tension has previously been suggested; however the proposed influence could not be demonstrated for mean inspiratory flow rates up to 1.4 liters/second. The mechanical tension is then translated into pressure, a process which is affected by the shape of the diaphragm dome. Finally the pressure expands the alveoli and causes air to flow, and the translation of pressure to volume depends on the elasto-viscous behaviour of the respiratory system. Consequently, there are many factors that may influence the tidal volume output obtained for a given increase in neural drive (inspiratory effort).

Evaluation of respiratory drive by measurements such as the rate of rise in pressure or lung volume is not reliable when, for example, the muscle length or the respiratory system impedance are affected by changes in the neuro-ventilatory efficiency. In a patient, airway resistance and elastance can change from one minute to another and muscle length is continuously altered.

OBJECTS AND SUMMARY OF THE INVENTION

An object of the present invention is therefore to eliminate the drawbacks of the prior art.

Another object of the present invention is to provide a closed loop system using:

(a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume;

(b) the inspiratory volume for a given EMG intensity; or

(c) a combination of (a) and (b);

in view of controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical (lung) ventilator; the closed loop ventilator system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency such that the neural drive remains stable at a desired target level. An alarm can also be used to detect changes in neuroventilatory efficiency in view of performing manual adjustments.

Another object of the present invention is to provide a closed-loop system responsive to the intensity of the diaphragm EMG measured immediately before the onset of inspiratory flow to quantify pre-inspiratory breathing effort in view of automatically or manually adjusting

a level of extrinsic positive end expiratory pressure (PEEP) applied to a patient in proportion to changes in EMG intensity of pre-inspiratory efforts. In this manner, the pre-ventilatory intensity of the diaphragm EMG can be maintained at a desired, minimum level such that the pre-inspiratory neural drive remains stable at a desired target minimal level. Determination of the duration from the onset of EMG to the onset of respiratory flow is also used for quantitative evaluation of the intrinsic PEEP, and to guide adjustment of the trigger sensitivity of the ventilator systems.

Different from pressure and ventilatory related indexes, the intensity of the EMG represents the temporal (mean MU (motor unit) rate coding) and spatial (MU recruitment) summation of action potentials and is obtained at the level of the sarcolemma muscle. The intensity of the EMG is therefore not affected by changes in the muscle's neuro-ventilatory coupling. In the present invention, the use of crural diaphragm EMG rests on the assumption that neural drive to the crural diaphragm is representative for the total respiratory drive. It is also based on the condition that neuromuscular transmission and innervation of the crural diaphragm are normal. For breathing with increased demand this assumption is well founded. Hence, the intensity of the EMG needed to produce a given inspiratory volume should express the efficiency relation between neural drive and volume output.

The objects, advantages and other features of the present invention will become more apparent upon reading of the following non restrictive description of a preferred embodiment thereof,

given by way of example only with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the appended drawings:

Figure 1 is a schematic representation of a set-up of an EMG analysis system;

Figure 2 is a section of oesophageal catheter on which an array of electrodes of the EMG analysis system of Figure 1 is mounted;

Figure 3 illustrates a section of oesophageal catheter on which a second embodiment of the array of electrodes is mounted;

Figure 4 is a graph showing a set of EMG signals of the diaphragm (EMGdi signals) detected by pairs of successive electrodes of the array of Figure 2;

Figure 5 is a flow chart showing a method for conducting a double subtraction technique of the EMGdi signals;

Figure 6 is a graph showing the distribution of correlation coefficients calculated for determining the position of the center of the

depolarizing region of the diaphragm along the array of electrodes of Figure 2;

Figure 7 is a schematic diagram illustrating in the time domain a double subtraction technique for improving the signal-to-noise ratio and to reduce an electrode-position-induced filter effect along the array of electrodes of Figure 2;

Figure 8a is a graph showing the power density spectrum of electrode motion artifacts, the power density spectrum of ECG, and the power density spectrum of EMGdi signals;

Figure 8b is a graph showing an example of transfer function for a filter to be used for filtering out the electrode motion artifacts, ECG, and the 50 or 60 Hz disturbance from electrical mains;

Figure 9 is a schematic diagram illustrating in the frequency domain stabilization by the double subtraction technique of the center frequency upon displacement of the center of the depolarizing region of the diaphragm along the array of electrodes of Figure 2;

Figure 10 is a schematic block diagram of a system according to the invention for controlling inspiratory assist by means of an EMGdi signal obtained with the above mentioned double subtraction technique and a measurement of the volume of air breathed by the patient by a commercially available system;

Figure 11 is a schematic block diagram of a system according to the invention (a) capable to determine the time delay from the onset of EMG to the onset of inspiratory flow and (b) using the level of pre-inspiratory effort obtained through the EMGdi signal intensity (common noise level subtracted) during a predetermined time period immediately preceding the onset of inspiratory flow to indicate the presence of "intrinsic PEEP" and to adjust the level of applied "extrinsic PEEP" and/or ventilator trigger sensitivity such that the level of pre-inspiratory effort is suppressed, i.e the EMGdi signal intensity (common noise level subtracted) during the above mentioned predetermined time period is close to zero;

Figure 12a is an exemplary graph of a patient's inspiratory flow versus time for quiet breathing in COPD (Chronic Obstructive Pulmonary Disease); and

Figure 12b is an exemplary graph of a patient's EMG RMS intensity versus time for quiet breathing in COPD.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Although the preferred embodiment of the present invention will be described in relation to a double subtracted EMGdi signal, it should be kept in mind that the concept of the present invention can be used with any respiratory muscle signal.

To measure EMG activity of the diaphragm 11 (EMGdi) of a human patient 14, an array of electrodes such as 12 (Figures 1 and 2) are mounted on the free end section 15 of an oesophageal catheter 13, with a constant inter-electrode distance **d** (Figure 2). As shown in Figure 1, the catheter 13 is introduced into the patient's oesophagus through one nostril or the mouth until the array of electrodes 12 is situated at the level of the gastroesophageal junction. The diaphragm 11 and/or the oesophagus slightly move during breathing of the patient 14 whereby the array of electrodes 12 also slightly moves about the diaphragm 11. As will be explained in the following description, automatic compensation for this displacement is provided for.

According to a preferred embodiment, an electrode 12 is mounted on the free end section 15 of the catheter 13 by winding stainless steel wire (not shown) around that catheter 13. The wound stainless steel wire presents a rough surface smoothed out by solder, which in turn is electroplated with nickel, copper and then gold or silver. Of course, it is within the scope of the present invention to use other electrode structures. Also, the electrodes 12 can possibly be applied to a nasogastric feeding tube (not shown) which is routinely introduced in intensive-care unit (ICU) patients.

Electric wires (not shown) interconnect each pair of successive electrodes such as 1-7 (Figure 2) with a respective one of a group of differential amplifiers 16. Obviously, these electric wires follow the catheter 13 from the respective electrodes 12 to the corresponding amplifiers 16, and are preferably integrated to the catheter 13. Preferably, the electric wires transmitting the EMGdi signals collected by

the various pairs 1-7 of electrodes 12 are shielded to reduce the influence of external noise, in particular disturbance from the 50 or 60 Hz current and voltage of the electrical mains.

The group of differential amplifiers 16 amplifies (first subtraction step of a so-called double subtraction technique) and band-pass filters each EMGdi signal. This first subtraction step may also be carried out in the personnal computer 19 when the amplifiers 16 are single-ended or equivalently designed amplifiers (monopolar readings).

In the example illustrated in Figures 1 and 2, the free end section 15 of the catheter 13 is provided with an array of eight electrodes 12 defining seven pairs 1, 2, 3, 4, 5, 6 and 7 of successive electrodes 12 respectively collecting seven different EMGdi signals. Although it has been found that EMG activity of the diaphragm (EMGdi) can be measured accurately with an oesophageal catheter 13 provided on the free end section 15 thereof with an array of eight electrodes 12, a different number and/or configuration of pairs of electrodes 12 can be contemplated depending on the patient's anatomy and movement of the diaphragm. Also, the pairs 1-7 do not need to be pairs of successive electrodes; as an example Figure 3 illustrates an array of nine electrodes to form seven overlapping pairs of electrodes 1-7.

A major problem in recording EMGdi signals is to maintain the noise level as low and as constant as possible. Since the electric wires transmitting the EMGdi signals from the electrodes 12 to the differential amplifiers 16 act as an antenna, it is crucial, as indicated in the foregoing description, to shield these electric wires to thereby protect the

EMGdi signals from additional artifactual noise. Also, the package enclosing the differential amplifiers 16 is preferably made as small as possible (miniaturized) and is positioned in close proximity to the patient to decrease as much as possible the distance between the electrodes 12 and the amplifiers 16.

The amplified EMGdi signals are sampled by a personal computer 19 through respective isolation amplifiers of a unit 18, to form signal segments of fixed duration. Unit 18 supplies electric power to the various electronic components of the differential and isolation amplifiers while ensuring adequate isolation of the patient's body from such power supply. The unit 18 also incorporates bandpass filters included in the respective EMGdi signal channels to eliminate the effects of aliasing. The successive EMGdi signal segments are then digitally processed into the personal computer 19 after analog-to-digital conversion thereof. This analog-to-digital conversion is conveniently carried out by an analog-to-digital converter implemented in the personal computer 19. The personal computer 19 includes a monitor 40 and a keyboard 31.

It is believed to be within the capacity of those of ordinary skill in the art to construct suitable differential amplifiers 16 and an adequate isolation amplifiers and power supply unit 18. Accordingly, the amplifiers 16 and the unit 18 will not be further described in the present specification.

An example of the seven EMGdi signals collected by the pairs 1-7 of successive electrodes 12 (Figures 1 and 2) and supplied to the computer 19 is illustrated in Figure 4.

As the diaphragm is generally perpendicular to the longitudinal axis of the oesophageal catheter 13 equipped with an array of electrodes 12, only a portion of the electrodes 12 are situated in the vicinity of the diaphragm. It is therefore important to determine the position of the diaphragm with respect to the oesophageal electrode array.

The portion of the crural diaphragm 11 which forms the muscular tunnel through which the oesophageal catheter 13 is passed is referred to the "diaphragm depolarizing region" (DDR). The thickness of the DDR is 20-30 mm. It can be assumed that, within the DDR, the distribution of active muscle fibers has a center from which the majority of the EMGdi signals originate, i.e. the "diaphragm depolarizing region center" (DDR center). Therefore, EMGdi signals detected on opposite sides of the DDR center will be reversed in polarity with no phase shift; in other words, EMGdi signals obtained along the electrode array are reversing in polarity at the DDR center.

Moving centrally from the boundaries of the DDR, EMGdi power spectrums progressively attenuate and enhance in frequency. Reversal of signal polarity on either side of the electrode pair 4 with the most attenuated power spectrum confirms the position from which the EMGdi signals originate, the DDR center.

Referring to Figure 5, the first task of the computer 19 is to determine the position of the center of the DDR along the array of electrodes 12. The center of the DDR is repeatedly determined at predetermined time intervals.

For that purpose, filtering step 505 removes from each EMGdi signal the motion artifacts, the electrocardiogram (ECG) component, and the disturbance from the electrical mains. Motion artifacts are induced by motion of the electrodes 12. More generally, motion artifacts are defined as a low frequency fluctuation of the EMGdi signals' DC level induced by mechanical alterations of the electrode metal to electrolyte interface i.e. changes in electrode contact area and/or changes in pressure that the tissue exerts on the electrode.

In step 501, the filtered EMGdi signals from step 505 are cross-correlated in pairs. As well known to those of ordinary skill in the art, cross-correlation is a statistical determination of the phase relationship between two signals and essentially calculates the similarity between two signals in terms of a correlation coefficient **r** (step 502). A negative correlation coefficient **r** indicates that the cross-correlated signals are of opposite polarities.

Figure 6 shows curves of the value of the correlation coefficient **r** versus the midpoint between the pairs of electrodes from which the correlated EMGdi signals originate. In this example, the inter-electrode distance is 10 mm. Curves are drawn for distances between the correlated pairs of electrodes 12 of 5 mm (curve 20), 10 mm (curve 21), 15 mm (curve 22) and 20 mm (curve 23). One can appreciate from Figure 5 that negative correlation coefficients **r** are obtained when EMGdi signals from respective electrode pairs situated on opposite sides of the electrode pair 4 are cross-correlated. It therefore appears that the change in polarity occurs in the region of electrode pair 4, which is confirmed by the curves of Figure 4. Accordingly, it can be assumed that

the center of the DDR is situated substantially midway between the electrodes 12 forming pair 4.

For example, the center of the DDR can be precisely determined by interpolation (step 503 of Figure 5) using a square law based fit of the three most negative correlation coefficients of curve 21 obtained by successive cross-correlation of the EMGdi signal segments from each electrode pair to the EMGdi signal segments from the second next electrode pair. Association of the center of the DDR to a pair of electrodes 12 provides a "reference position" from which to obtain EMGdi signal segments within the DDR. Such control is essential in overcoming the artifactual influence of perpendicular bipolar electrode filtering on the EMGdi power spectrum.

It has been experimentally demonstrated that EMGdi signals recorded in the oesophagus are satisfactory as long as they are obtained from electrode pairs (with an inter-electrode distance situated between 5 and 20 mm) positioned at a distance situated between 5 and 30 mm on the opposite sides of the DDR center (the inter-pair distance being therefore situated between 5 and 30 mm). Although EMGdi signals obtained from these positions offers a clear improvement in acceptance rate, the signal-to-noise ratio during quiet breathing still tends to remain unsatisfactorily low. The EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

For example, in Figure 4, the EMGdi signals originating from the electrode pairs 3 and 5 situated respectively 10 mm below and 10 mm above the DDR are strongly inversely correlated at zero time delay. In contrast to the inversely correlated EMGdi signals, the noise components for electrode pairs 3 and 5 are likely to be positively correlated. Hence, as illustrated in Figure 7, subtraction of the EMGdi signals 24 and 25 from electrode pairs 3 and 5 will result into an addition of the corresponding EMGdi signals (signal 26 of Figure 6) and into a subtraction, that is an elimination of the common noise components. This technique will be referred to as "the double subtraction technique" (step 504 of Figure 5). Again, the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

Subtraction step 504 (second subtraction step of the double subtraction technique) can be carried out either in the time domain, or after conversion of signals 24 and 25 in the frequency domain. Double subtraction technique can be performed by subtracting other combinations of signals, for example by subtracting the EMGdi signal segments from electrode pair 2 from the EMGdi signal segments from electrode pair 5 (Figure 4), by subtracting signal segments from electrode pair 6 from the signal segments from electrode pair 3 and by adding these differences, etc. What is important is to subtract two signals of opposite polarities obtained in the vicinity of the muscle. More than two signal pairs of opposite polarities can be used in the double subtraction. Again,

the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

The double subtraction technique is carried out in step 504 on the pair of EMGdi signals (for example the signals from electrode pairs 3 and 5 shown in Figure 4) identified in step 503, after appropriate filtering of these EMGdi signals in step 505. Still again, the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

The graph of Figure 8a shows the power density spectrum of the above defined electrode motion artifacts, the power density spectrum of ECG, and the power density spectrum of EMGdi signals. The graph of Figure 8b shows an example of transfer function for a filter (the dashed line showing the optimal transfer function, and the solid line the transfer function implemented by the inventors) to be used in step 505 for filtering out the electrode motion artifacts, ECG, and the 50 or 60 Hz disturbance from the electrical mains. Processing of the EMGdi signals by the computer 19 to follow as closely as possible the optimal transfer function of Figure 8b will conduct adequately filtering step 505.

Therefore, double-subtracted signal segments 509 are obtained at the output of step 504 by subtracting the EMGdi signal segments from the pair of electrodes 12 in optimal location above the diaphragm from the EMGdi signal segments from the pair of electrodes 12 in optimal location below the diaphragm. More than two signal pairs of opposite polarities can be used in the double subtraction. Again, the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

Referring back to Figure 5, step 506 calculates the RMS (root-mean-square) or equivalent or similar value 510 of the double-subtracted signal segments 509 produced in step 504. The increase in intensity obtained with the double subtraction technique is associated with a twofold increase in RMS values. RMS values obtained with the double subtraction technique are closely and linearly related to the original signals. It should be kept in mind that the RMS value can be replaced by any other value representative of the strength of the double-subtracted signal segments 509.

The digital RMS signal segment value 510 calculated by the computer 19 in step 506 is finally digital-to-analog converted to an on-line analog RMS value 508 (step 507) in view of controlling a lung ventilator 54 (Figure 10). It should be mentioned that it is within the scope of the present invention to supply a digital value 508.

The double subtraction technique compensates for the changes in signal strength and frequency caused by movement of the diaphragm 11 (Figure 1) and/or the oesophagus during breathing of the patient 14 causing movement of the array of electrodes 12 with respect to the diaphragm 11. Referring to Figure 9, off center of the array of electrodes 12 (electrode-position-induced filter effect) causes a variation of center frequency values due to filtering (see curves 27 and 28) for the EMGdi signals from the electrode pairs 3 and 5. The double subtraction technique eliminates such variation of center frequency values as indicated by curve 29 as well as variation of signal strength. Therefore, the reciprocal influence of the position of the DDR center on the EMGdi signal frequency content is eliminated by the double subtraction technique.

It has been found that the double subtraction technique may improve the signal-to-noise ratio by more than 2 dB and reduce an electrode-position-induced filter effect. Double subtraction technique is also responsible for a relative increase in acceptance rate by more than 30%.

Noise of non diaphragmatic origin or artifactual signals are strongly correlated at zero time delay and equal in polarity between all pairs of electrodes 12. Hence, this noise of non diaphragmatic origin or artifactual signals appear as a common mode signal for all electrode pairs and therefore, are substantially reduced by the double subtraction technique.

In the following description, it should be considered that the flow and volume of air breathed by the patient can be measured by any commercially available system.

Neuro-ventilatory efficiency:

The neuro-ventilatory efficiency is obtained by relating the diaphragm EMGdi signal intensity to changes in lung volume, or by relating the lung volume to changes in diaphragm EMGdi signal intensity. Since the relationship between the diaphragm EMGdi signal intensity and the lung volume is not linear, this non-linearity is minimized by expressing:

- the intensity of the diaphragm EMGdi signal for a given volume change from end-expiratory lung volume, for example the EMGdi signal intensity obtained during 400 ml inspiration starting from end-expiratory lung volume (in the present disclosure, intensity is intended to encompass the mean, peak, median and total RMS intensity of the diaphragm EMGdi signal); or

- the lung volume obtained at a given diaphragm EMGdi signal intensity.

A relatively small tidal lung volume is suitable because the relationship between diaphragm EMGdi signal intensity and lung volume is relatively linear at this low range. Secondly, the use of a fixed, given tidal volume or diaphragm EMGdi signal intensity will protect against the non-linear influences and allows for a reliable estimation of relative changes in neuro-ventilatory efficiency.

In this manner, a ventilatory efficiency index expressing:

- the EMGdi signal intensity for a given inspiratory lung volume starting from the end-expiratory lung volume; or

- the lung volume for a given diaphragm EMGdi signal intensity;

is calculated. If the EMGdi signal intensity for the above mentioned given inspiratory lung volume or the lung volume for the above mentioned given diaphragm EMGdi signal intensity is changing, the above indicated index will also change and this change can be expressed in percentage (%). For example, using the diaphragm EMGdi signal intensity for the above mentioned fixed, given inspiratory lung volume, an increased EMGdi signal intensity for the above mentioned given inspiratory lung volume will increase the index but will express a reduction in the neuro-ventilatory efficiency, and a decreased EMGdi signal intensity for that given inspiratory lung volume will reduce the index but will express an improvement of the neuro-ventilatory efficiency.

In the following description, an example using the EMGdi signal intensity for a fixed, given inspiratory lung volume will be given. However, it is within the scope of the present invention to use the lung volume for a fixed, given diaphragm EMGdi signal intensity.

Referring now to Figure 10 a preferred, practical embodiment is described. A neuro-ventilatory efficiency computation device 601 receives the signal 508 of Figure 5 as well as the given, fixed inspiratory lung volume. Device 601 comprises a unit 602 for determining

the intensity of the signal 508 for the given inspiratory lung volume. Although it is not illustrated, it is within the scope of the present invention to calculate, in unit 602, the peak, mean, median or any other intensity measure of signal 508 for the given inspiratory lung volume. If the intensity of signal 508 for the given inspiratory lung volume has increased at least by a given percentage (step 603), i.e. the neuro-ventilatory efficiency index has increased at least by said given percentage, the pressure, flow, or volume assist unit 604 is controlled by a unit 606 in view of increasing the magnitude of the pressure assist to the patient by a preset increment until the intensity of the signal 508 for the given inspiratory lung volume is restored to a predetermined, preset value.

Still referring to Figure 10, if the intensity for the given inspiratory lung volume has decreased at least by a given percentage (step 607), i.e. the neuro-ventilatory efficiency index has decreased at least by said given percentage, the pressure assist unit 604 is controlled by the unit 608 in view of decreasing the magnitude of the pressure assist by a preset increment until the intensity of the signal 508 for the given inspiratory lung volume is restored to the predetermined, preset value. Although it is not illustrated, it is within the scope of the present invention to calculate, in unit 602, the peak, mean, median or any other intensity measure of signal 508 for the given inspiratory lung volume, instead of the intensity of this signal. Also, the signals at the outputs of the units 606 and 608 can be used to generate an alarm or to manually adjust the pressure, flow or volume assist to the patient.

The response time is adjustable. The time base used to calculate trends in the EMG intensity for a given volume or vice versa

and used for the corrections is relatively slow (minutes) and the levels of applied support can be limited within a safe range. Again, an alarm can be generated or the pressure assist can be manually or automatically adjusted.

The pressure, flow, or volume assist unit 604 can be any device which can be controlled to generate any airway pressure of adjustable magnitude, for example any source of compressed gas, or a flow or volume pump. Of course, airway 605 refers to or, to the least, includes the patient's respiratory airway.

In this manner, the pressure assist unit 604 provides a pressure, flow, or volume assist that is adjusted in proportion to changed in neuro-ventilatory efficiency which is the EMGdi signal intensity at a given lung volume or vice versa. The pressure, flow, or volume assist unit continuoulsy operates to maintain a tracheal pressure, flow or volume that is adjusted in proportion to changes in neuro-ventilatory efficiency which is the EMGdi signal intensity at a given lung volume or vice versa.

Pre-inspiratory breathing effort:

A common problem with mechanically ventilated patients is that the patients' inspiratory effort will not immediately cause an inspiratory airflow so called "intrinsic PEEP" or "auto PEEP" which leads to a decrease in the neuro-ventilatory efficiency. The effect of "intrinsic PEEP" can be counteracted by the application of an "extrinsic PEEP" . However, there are no easy applicable techniques to determine when the applied level of "extrinsic PEEP" is adequate. The level of pre-inspiratory

effort obtained through the EMGdi signal intensity (common noise level subtracted) during for example a 100 milliseconds (ms) period immediately preceding the onset of inspiratory flow can be used to indicate the presence of "intrinsic PEEP", and the level of applied "extrinsic PEEP" can be adjusted such that the level of pre-inspiratory effort is suppressed i.e the EMGdi signal intensity (common noise level subtracted) during the above mentioned 100 ms period before onset of inspiratory flow is close to zero. A feedback loop can then be used to maintain the level of pre-inspiratory effort suppressed by adjusting as explained above the level of "extrinsic PEEP".

Just a word to mention that the above mentioned period of 100 ms can be replaced by a longer or shorter time period immediately preceding the onset of inspiratory flow or by the neuro-ventilatory delay 800 (Figure 12b), i.e. the time period between the onset of EMG 801 (Figure 12b) and the onset of inspiratory flow 802 (Figure 12a).

Figure 11 of the appended drawings illustrates a preferred, practical embodiment 700.

In the embodiment 700, an integrator 713 is responsive to the RMS EMG signal 508 to continuously calculate the EMG intensity for the above mentioned 100 ms period or neuro-ventilatory delay 800.

Embodiment 700 also comprises an inspiratory flow detector 702 responsive to the patient's inspiratory flow 703 measured, as indicated in the foregoing description, through any commercially

available system, to produce an output signal 705 representative of EMG activity.

The embodiment 700 of Figure 11 also comprises a neuro-ventilatory delay calculator 704 responsive to (a) the detection of a RMS EMG signal intensity higher than the common noise level (5%), and (b) the detection of the onset of inspiratory flow by the detector 702 to calculate the neuro-ventilatory delay 800 (Figure 12b).

A detector 714 is responsive to the EMG intensity calculated by the integrator 713 to detect the level of EMG intensity 803 (Figure 12b) at the onset of inspiratory flow 802 (Figure 12a) to trigger an alarm 716 when the level of the EMG intensity 803 at the onset of inspiratory flow 802 is higher than a given limit (detector 715). Upon triggering of the alarm 716, the level of applied "extrinsic PEEP" is either automatically or manually increased (device 708).

The detector 714 is responsive to the EMG intensity calculated by the integrator 713 to detect the level of EMG intensity 803 (Figure 12b) at the onset of inspiratory flow 802 (Figure 12a) to trigger an alarm 720 when the level of the EMG intensity 803 at the onset of inspiratory flow 802 is lower than a given limit (detector 719). Upon triggering of the alarm 720, the level of applied "extrinsic PEEP" is either automatically or manually decreased (device 711).

It should be mentioned that feedback from the neuro-ventilatory delay or pre-inspiratory EMG activity can also be used to adjust the sensitivity of the ventilators trigger functions.

Again, the time base used for these corrections is preferably relatively slow (minutes) and the levels of "extrinsic PEEP" can be limited within a safe range.

The pressure assist unit 604 can be any device which can be controlled to generate any airway flow and/or pressure of adjustable magnitude, for example any source of compressed gas, or a flow or volume pump.

In this manner, the delay from the beginning of the mechanically ventilated patients' inspiratory effort to the onset of the inspiratory assist will be minimized.

Although the present invention has been described hereinabove with reference to preferred embodiments thereof, these embodiments can be modified at will, within the scope of the appended claims, without departing from the spirit and nature of the subject invention.

CLAIMS

1. A closed loop system for controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical lung ventilator, comprising:

means for measuring (a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume, (b) the inspiratory volume for a given EMG intensity, and/or (c) a combination of (a) and (b); and

means for controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical lung ventilator in response to measurement of (a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume, (b) the inspiratory volume for a given EMG intensity, and/or (c) the combination of (a) and (b);

wherein the closed loop system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency such that the neural drive remains stable at a desired target level.

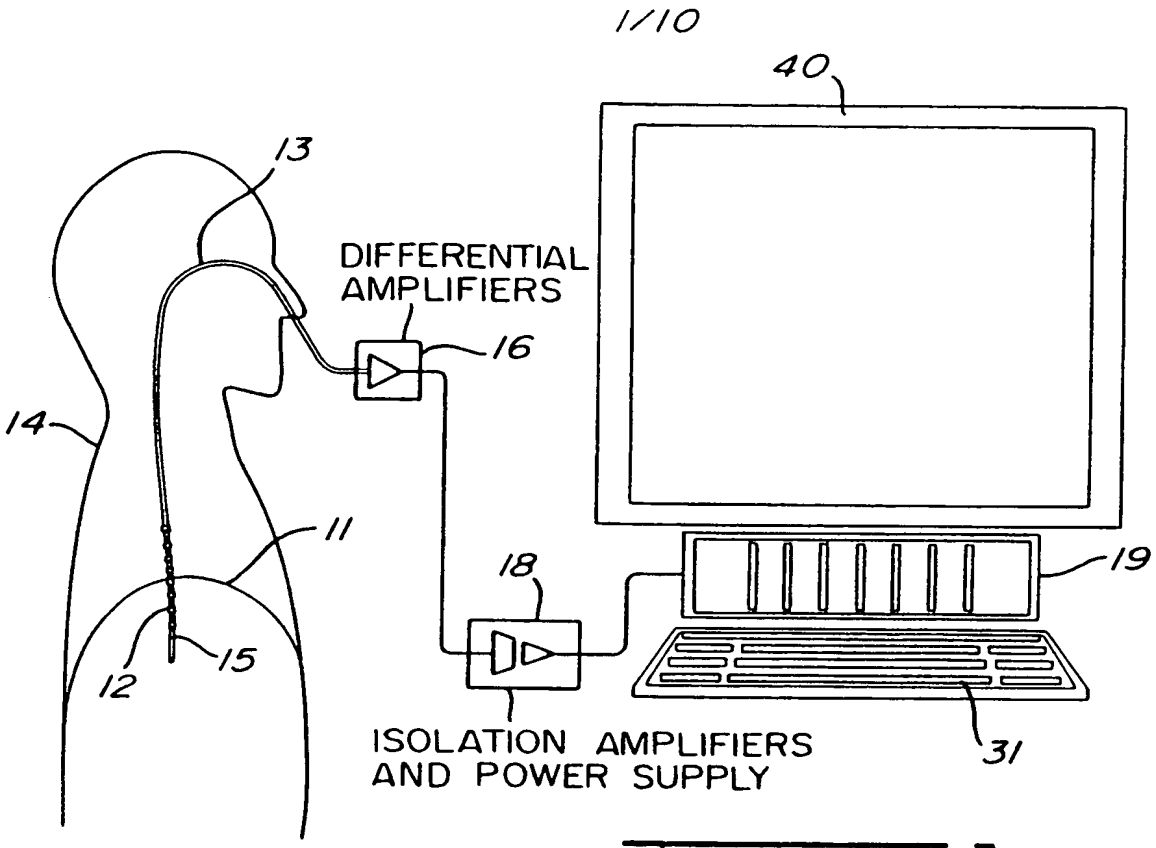
1/10
40
13
DIFFERENTIAL
AMPLIFIERS
16
14
11
18
19
12
15
ISOLATION AMPLIFIERS
AND POWER SUPPLY
31

Fig. 1

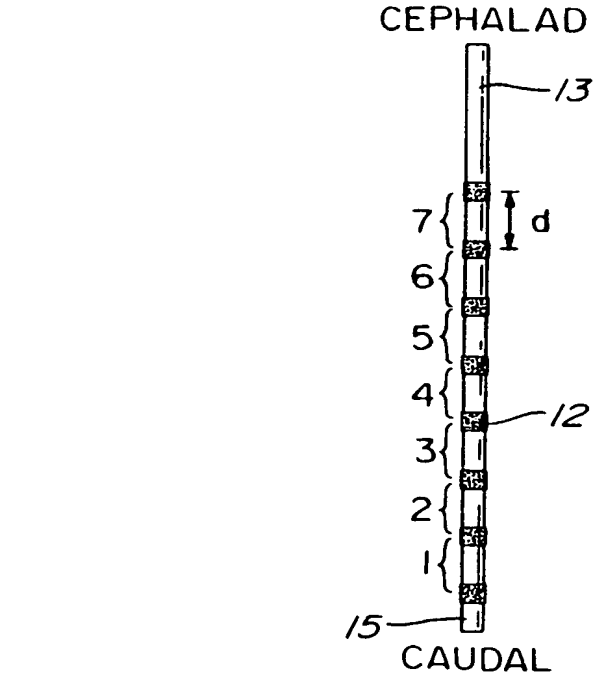
CEPHALAD
13
7
d
6
5
4
12
3
2
1
15
CAUDAL

Fig. 2

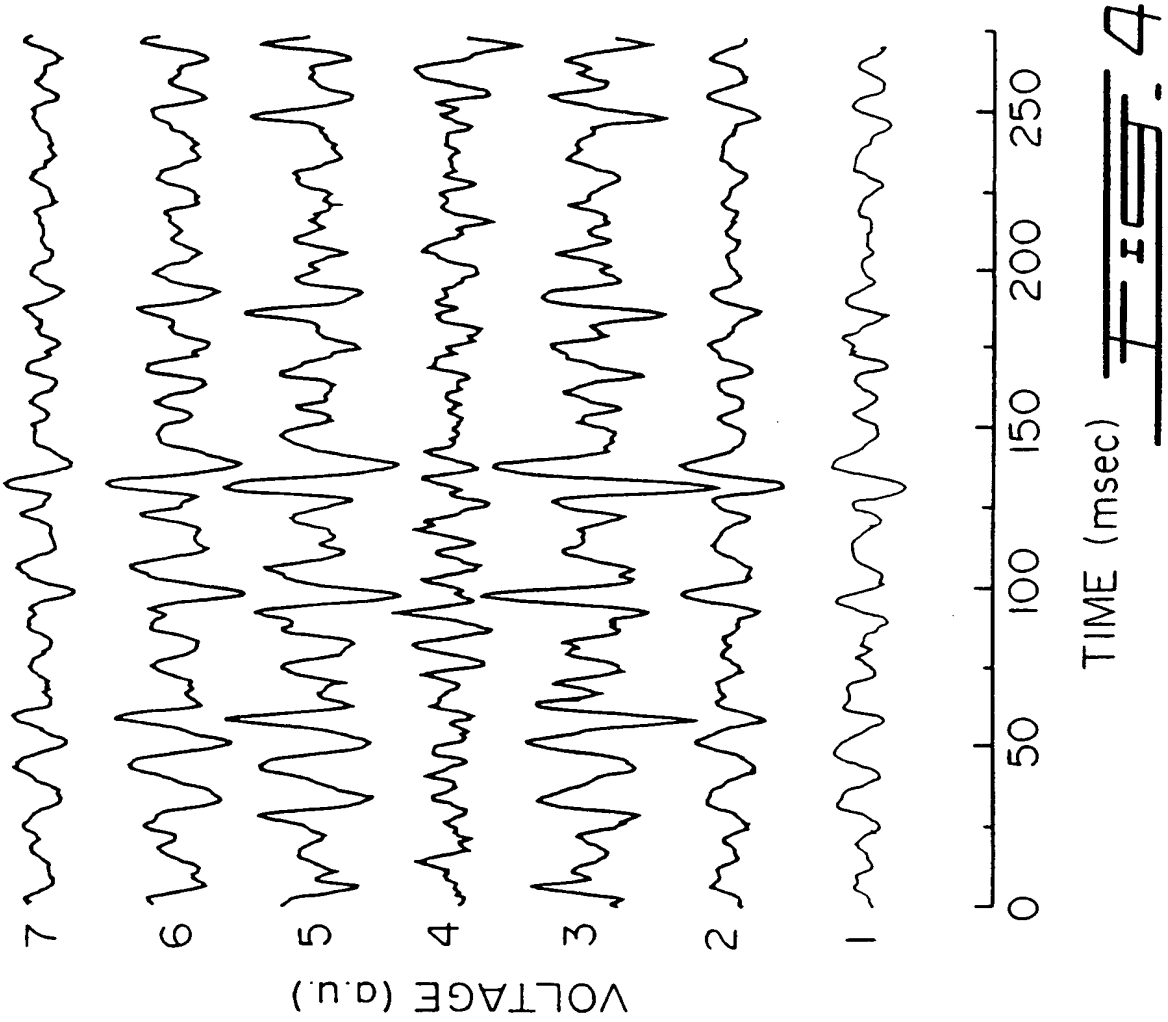
7
6
5
4
3
2
1
VOLTAGE (a.u.)
0
50
100
150
200
250
TIME (msec)

FIG. 4

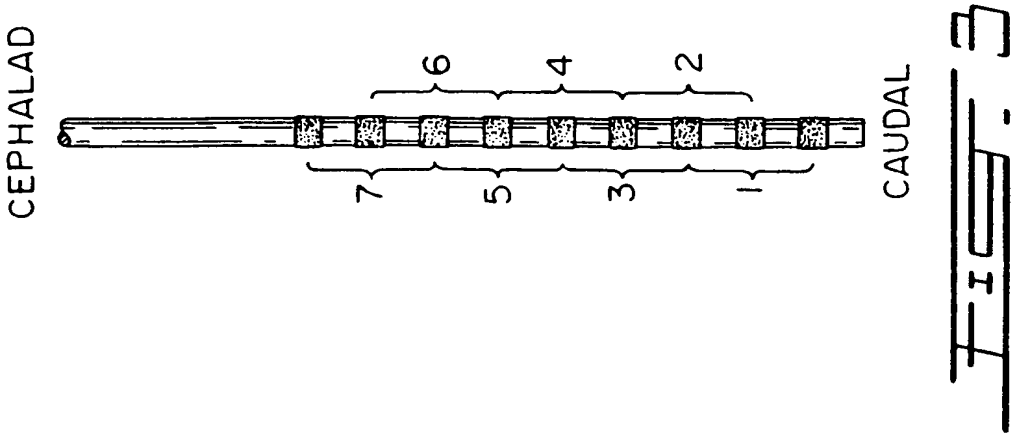
CEPHALAD
CAUDAL
7
6
5
4
3
2
1

FIG. 3

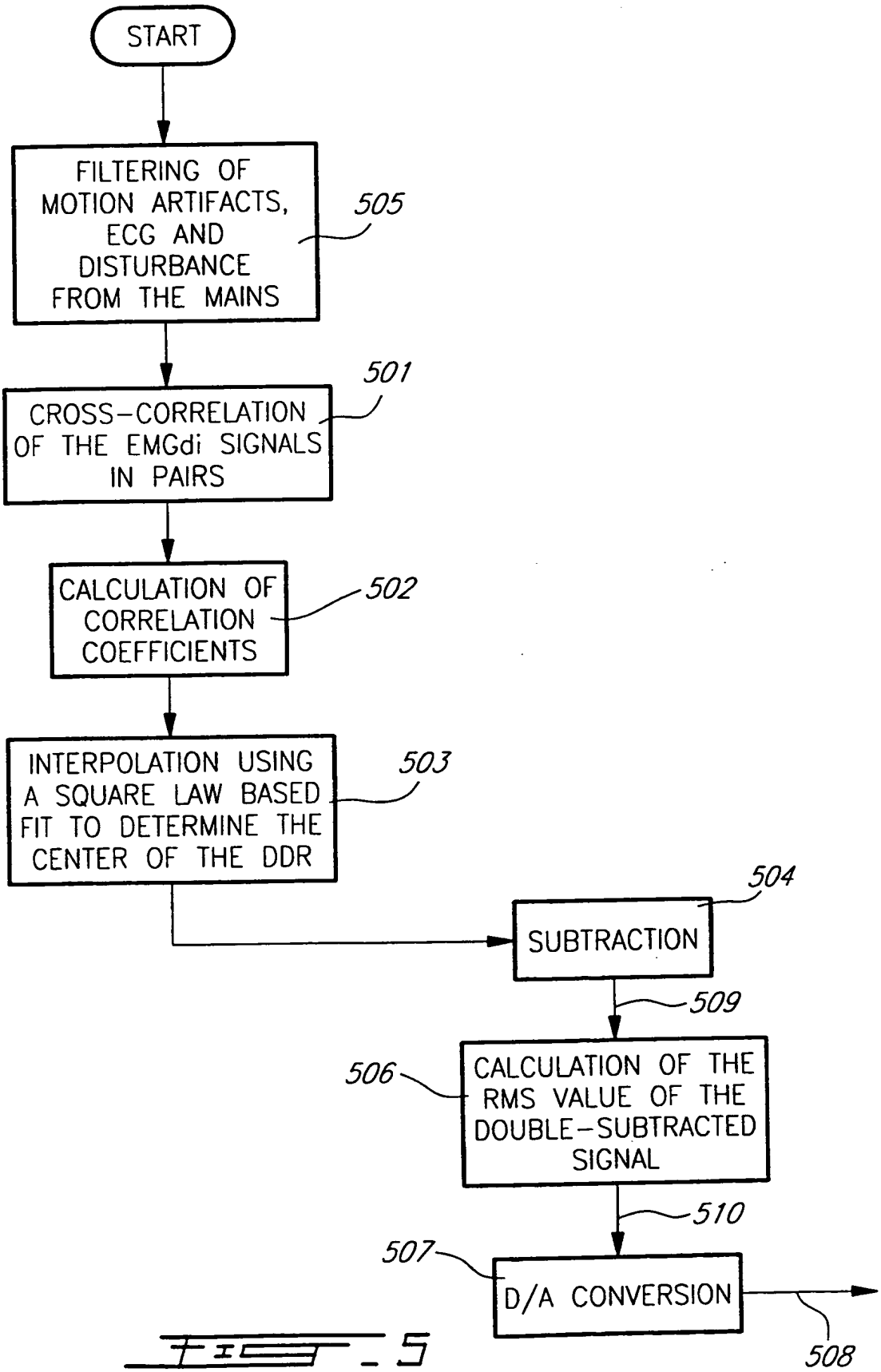
START
FILTERING OF MOTION ARTIFACTS, ECG AND DISTURBANCE FROM THE MAINS
505
CROSS-CORRELATION OF THE EMGdi SIGNALS IN PAIRS
501
CALCULATION OF CORRELATION COEFFICIENTS
502
INTERPOLATION USING A SQUARE LAW BASED FIT TO DETERMINE THE CENTER OF THE DDR
503
504
SUBTRACTION
509
506
CALCULATION OF THE RMS VALUE OF THE DOUBLE-SUBTRACTED SIGNAL
510
507
D/A CONVERSION
508

FIG. 5

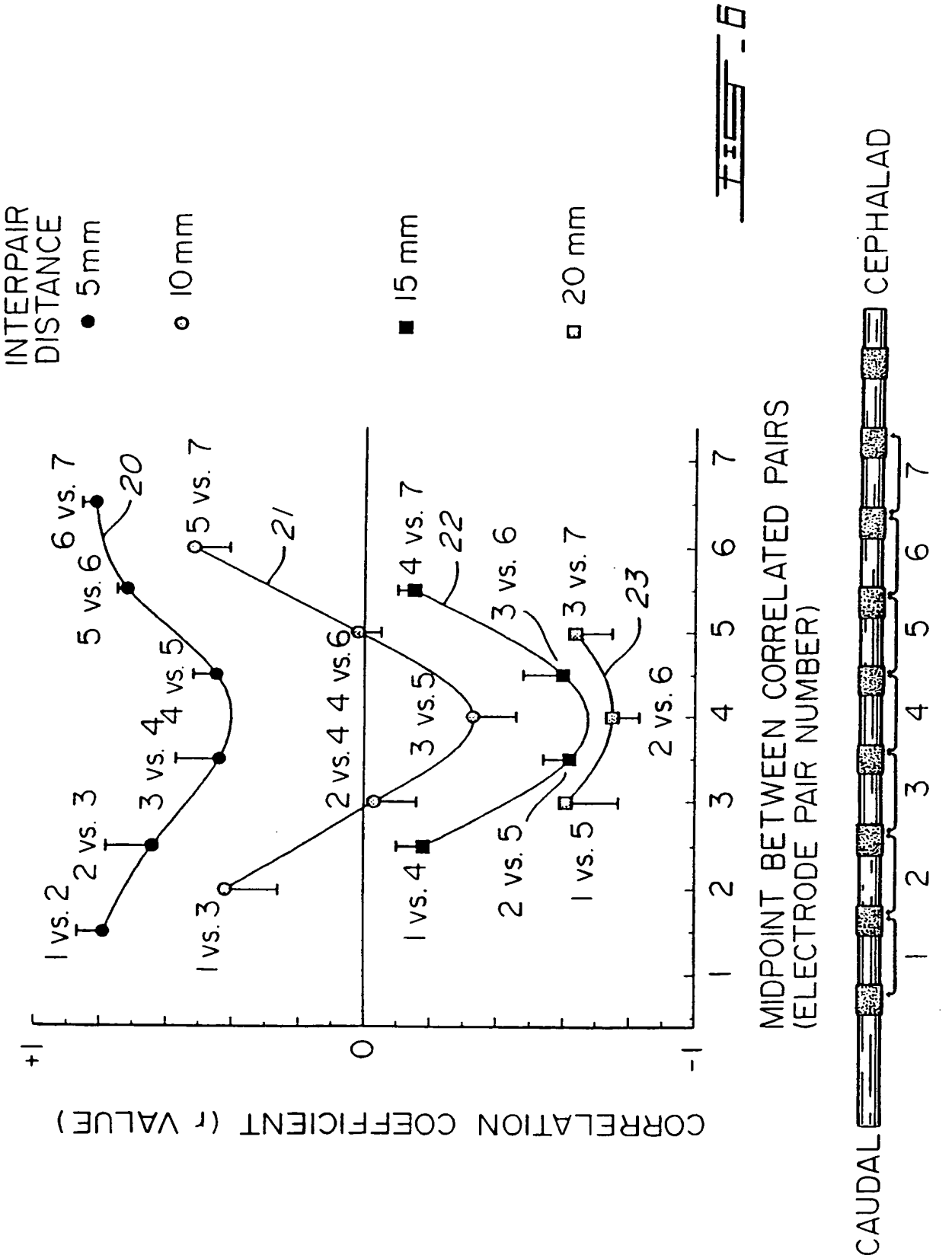
INTERPAIR DISTANCE
5 mm
10 mm
15 mm
20 mm
CORRELATION COEFFICIENT (r VALUE)
+1
0
-1
1 vs. 2
2 vs. 3
3 vs. 4
4 vs. 5
5 vs. 6
6 vs. 7
20
1 vs. 3
2 vs. 4
3 vs. 5
4 vs. 6
5 vs. 7
21
1 vs. 4
2 vs. 5
3 vs. 6
4 vs. 7
22
1 vs. 5
2 vs. 6
3 vs. 7
23
1 2 3 4 5 6 7
MIDPOINT BETWEEN CORRELATED PAIRS
(ELECTRODE PAIR NUMBER)
CAUDAL
CEPHALAD
1 2 3 4 5 6 7

FIG. 6

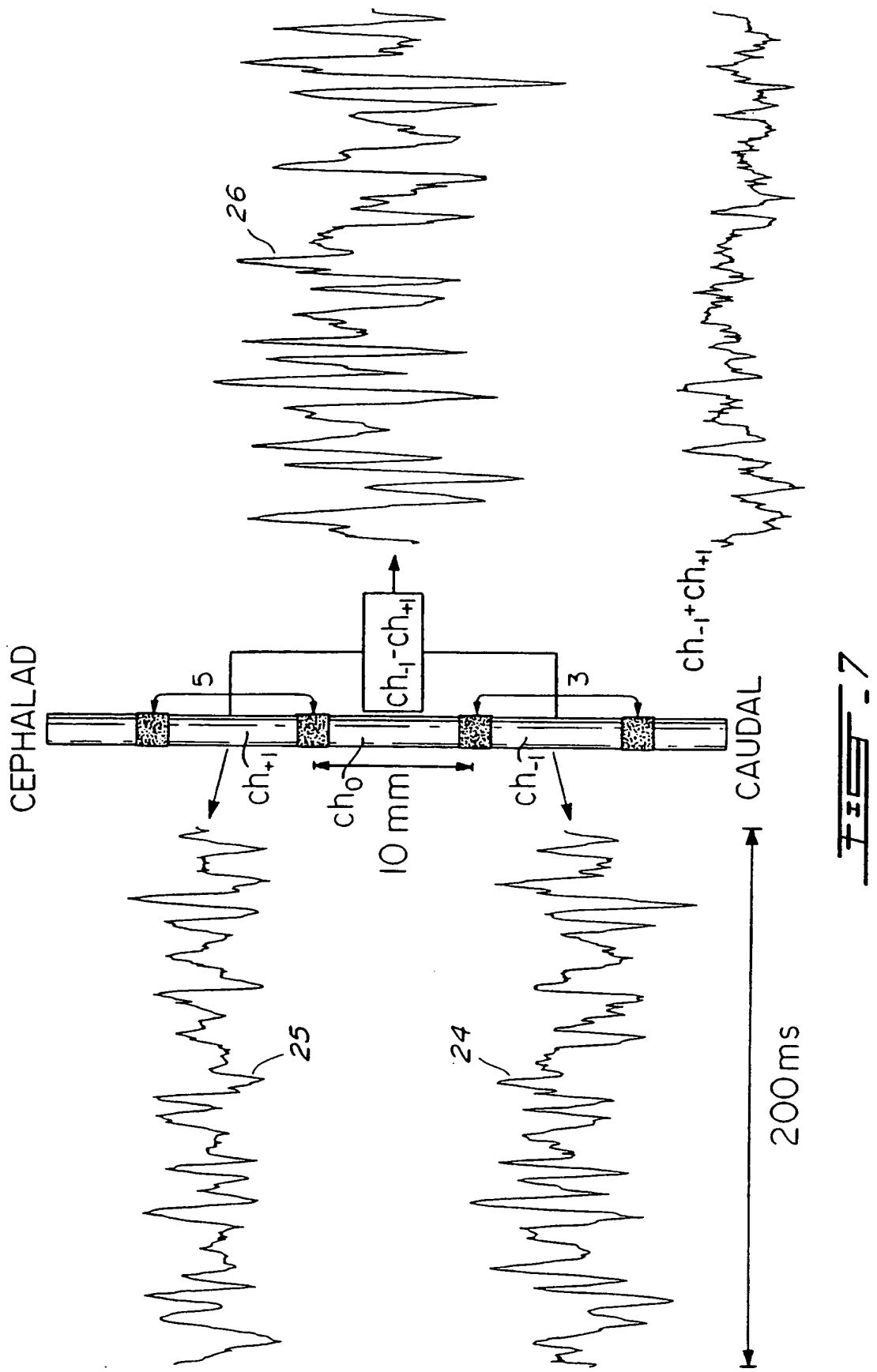
26
$ch_{-1}+ch_{+1}$
$ch_{-1}-ch_{+1}$
5
3
CEPHALAD
CAUDAL
ch_{+1}
ch_0
ch_{-1}
10 mm
25
24
200ms

FIG. 7

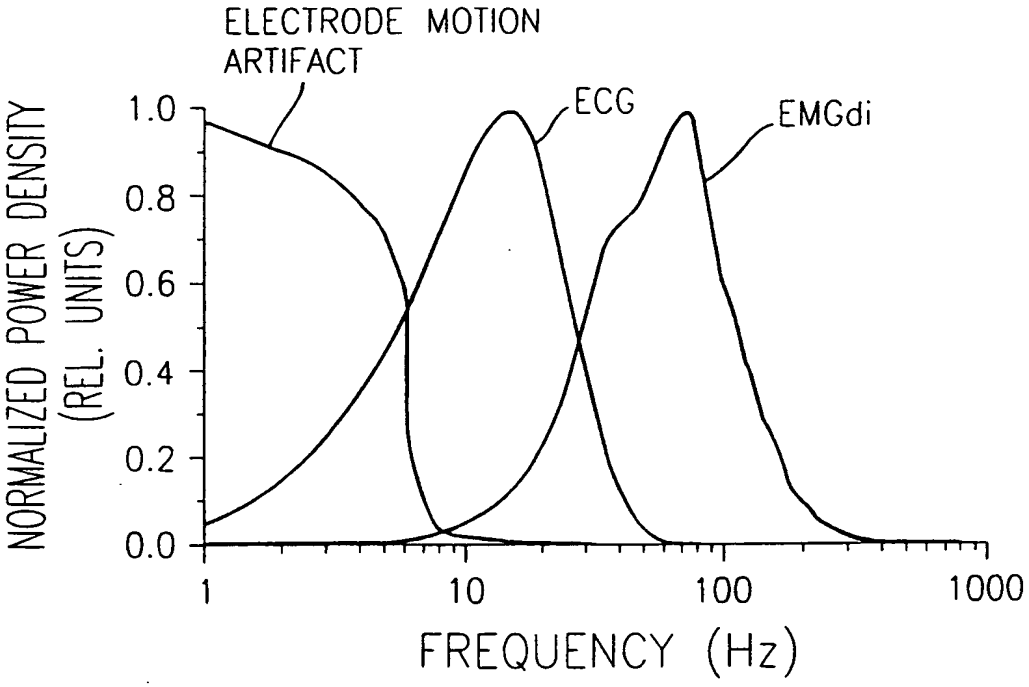
ELECTRODE MOTION ARTIFACT
ECG
EMGdi
NORMALIZED POWER DENSITY (REL. UNITS)
1.0
0.8
0.6
0.4
0.2
0.0
1
10
100
1000
FREQUENCY (Hz)

Fig 8a

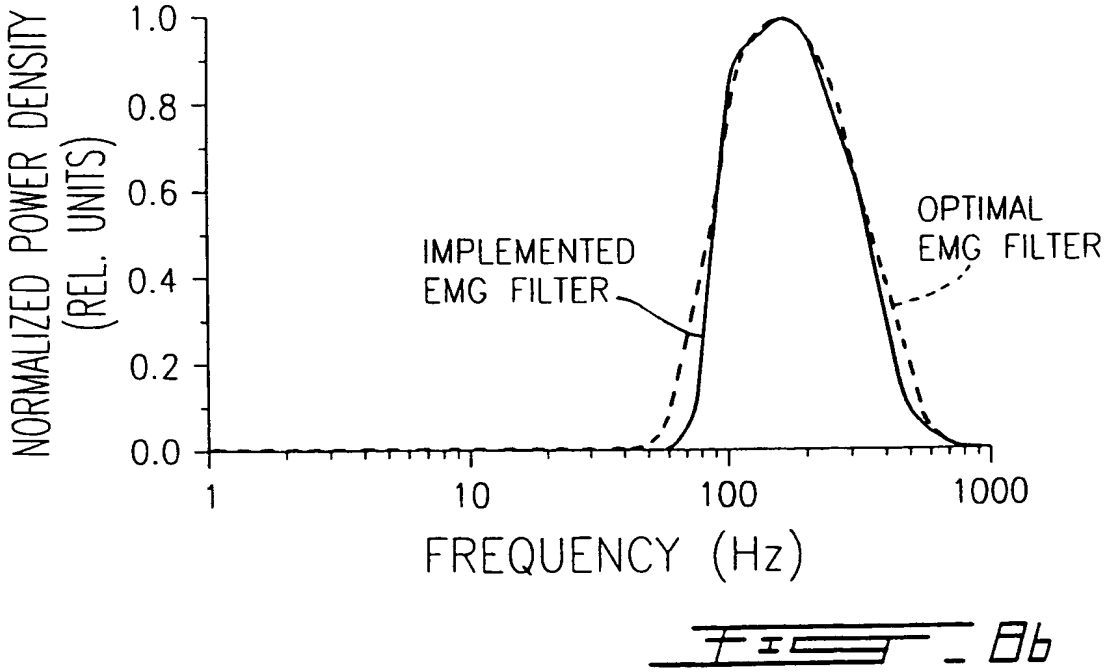
NORMALIZED POWER DENSITY (REL. UNITS)
1.0
0.8
0.6
0.4
0.2
0.0
IMPLEMENTED EMG FILTER
OPTIMAL EMG FILTER
1
10
100
1000
FREQUENCY (Hz)

Fig 8b

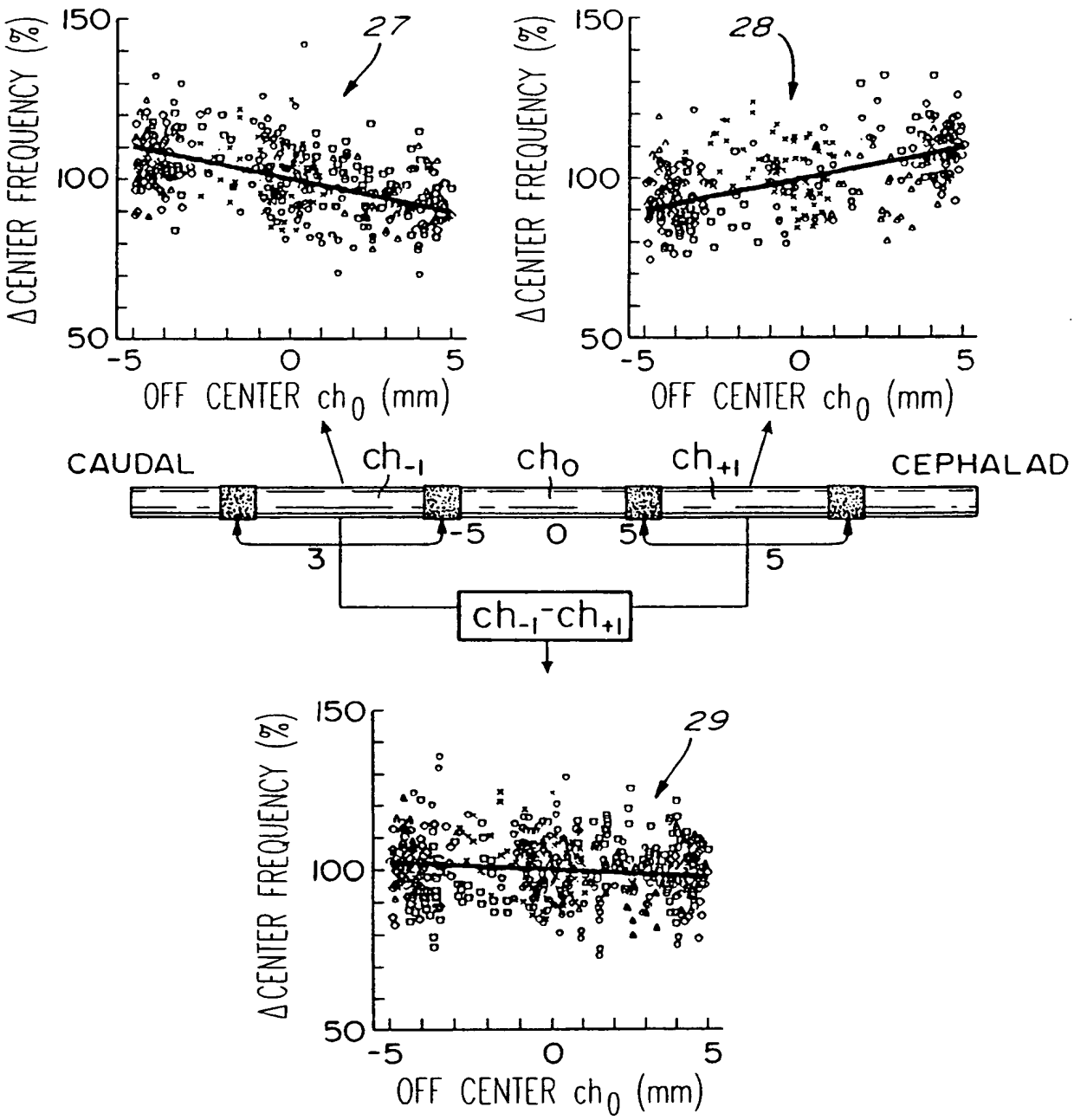
ΔCENTER FREQUENCY (%)
150
100
50
27
-5
0
5
OFF CENTER ch0 (mm)
28
CAUDAL
CEPHALAD
ch-1
ch0
ch+1
3
-5
0
5
5
ch-1-ch+1
29

FIG 9

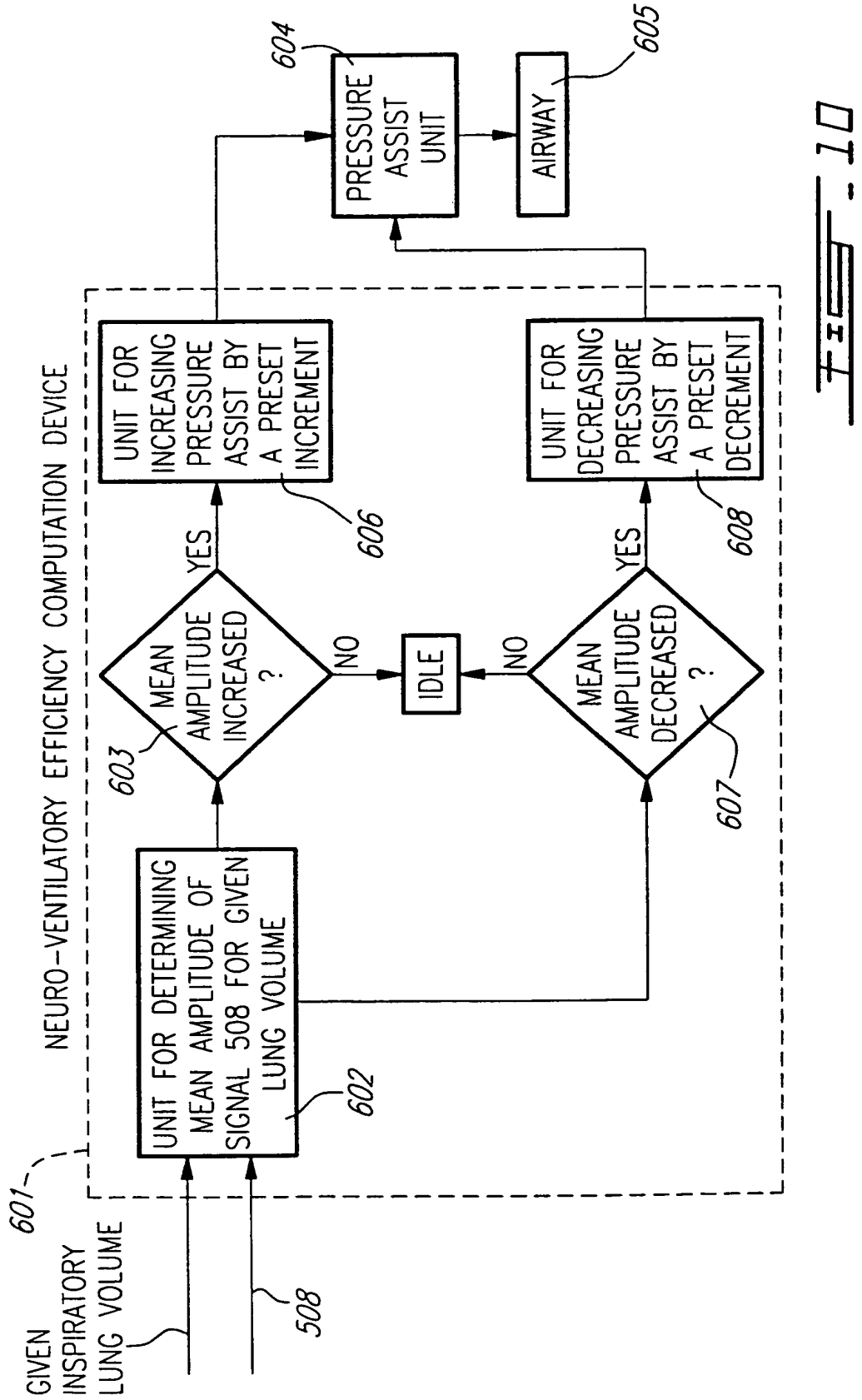
GIVEN INSPIRATORY LUNG VOLUME
508
601
NEURO-VENTILATORY EFFICIENCY COMPUTATION DEVICE
UNIT FOR DETERMINING MEAN AMPLITUDE OF SIGNAL 508 FOR GIVEN LUNG VOLUME
602
MEAN AMPLITUDE INCREASED ?
603
YES
NO
IDLE
MEAN AMPLITUDE DECREASED ?
607
YES
NO
UNIT FOR INCREASING PRESSURE ASSIST BY A PRESET INCREMENT
606
UNIT FOR DECREASING PRESSURE ASSIST BY A PRESET DECREMENT
608
PRESSURE ASSIST UNIT
604
AIRWAY
605

FIG - 10

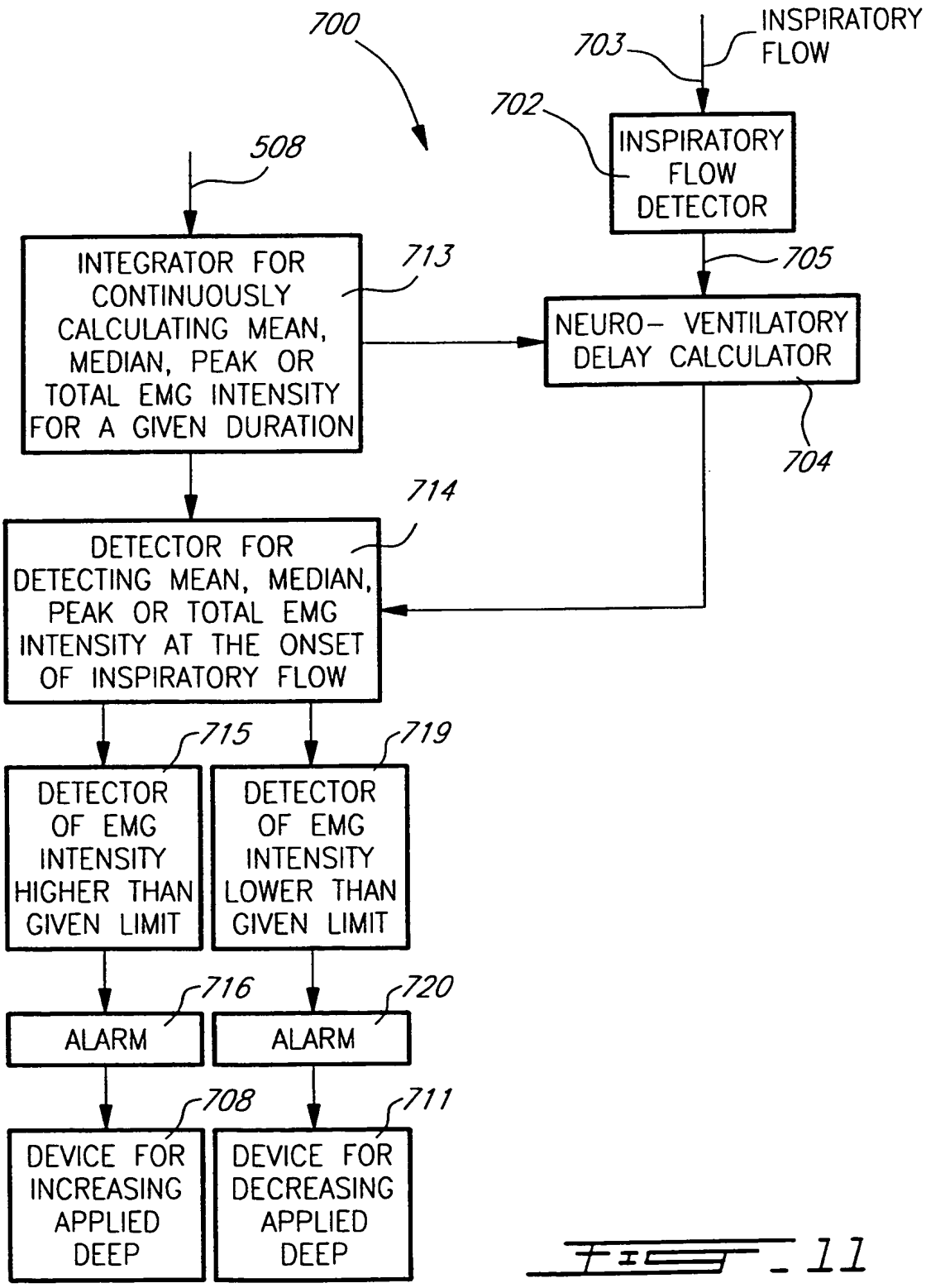
700
703
INSPIRATORY FLOW
702
INSPIRATORY FLOW DETECTOR
508
705
INTEGRATOR FOR CONTINUOUSLY CALCULATING MEAN, MEDIAN, PEAK OR TOTAL EMG INTENSITY FOR A GIVEN DURATION
713
NEURO- VENTILATORY DELAY CALCULATOR
704
714
DETECTOR FOR DETECTING MEAN, MEDIAN, PEAK OR TOTAL EMG INTENSITY AT THE ONSET OF INSPIRATORY FLOW
715
719
DETECTOR OF EMG INTENSITY HIGHER THAN GIVEN LIMIT
DETECTOR OF EMG INTENSITY LOWER THAN GIVEN LIMIT
716
720
ALARM
ALARM
708
711
DEVICE FOR INCREASING APPLIED DEEP
DEVICE FOR DECREASING APPLIED DEEP

Fig. 11

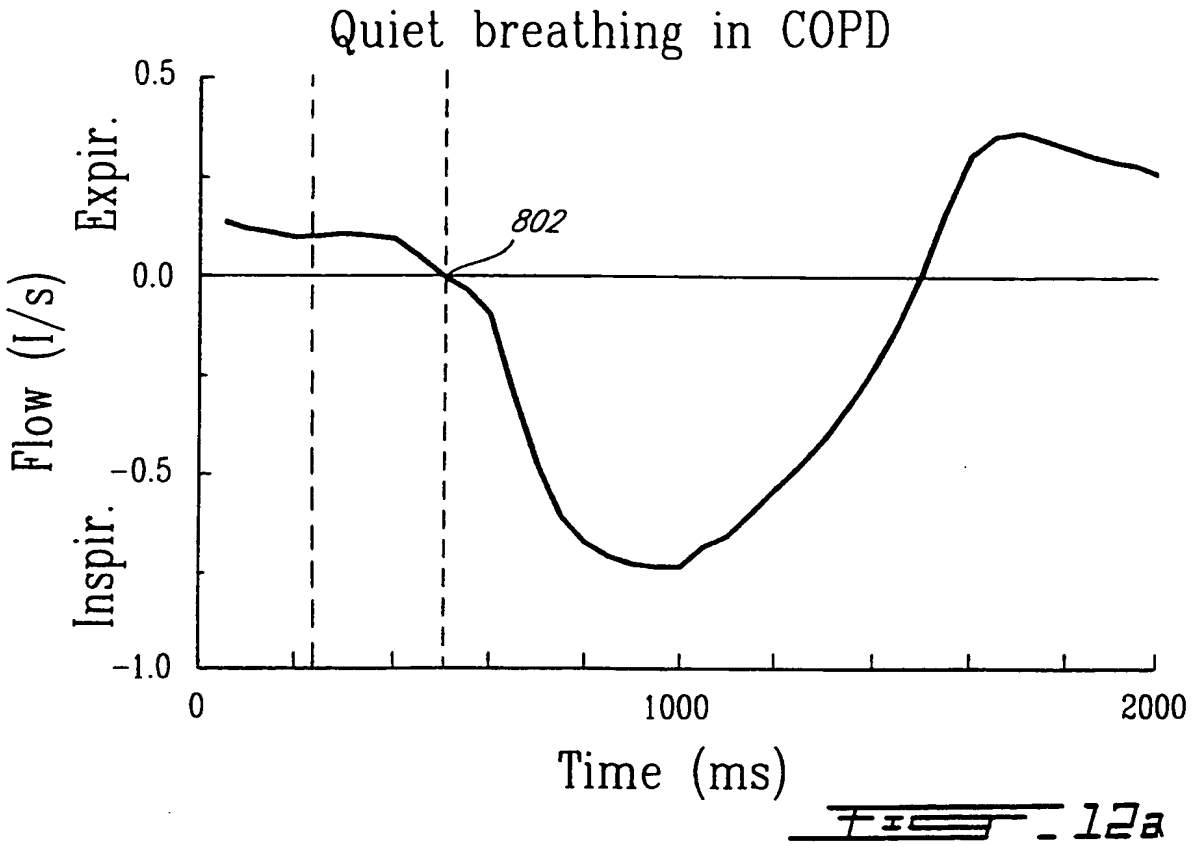

Fig 12a

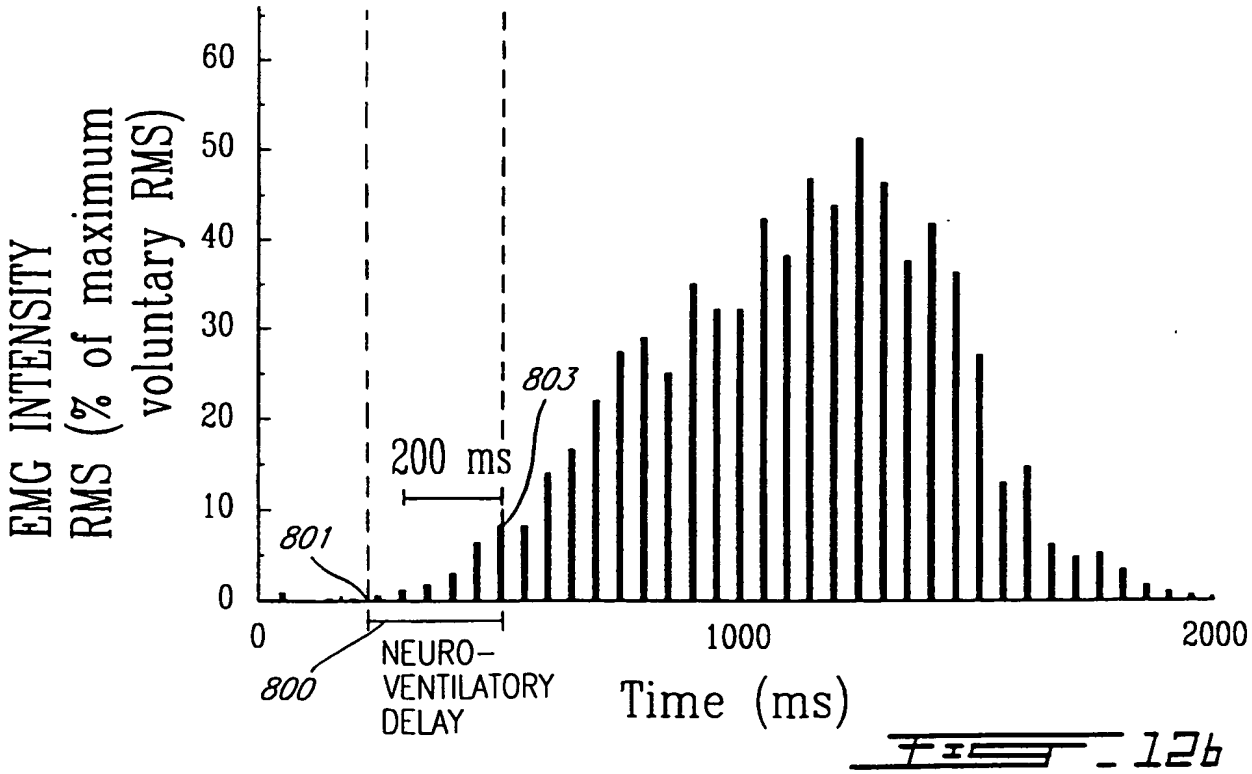

Fig 12b

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 99/00529

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M16/00 A61B5/0488

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	E. AGOSTINI ET AL.: "Electromyography of the diaphragm in man and transdiaphragmatic pressure" JOURNAL OF APPLIED PHYSIOLOGY, vol. 15, 1960, pages 1093-1097, XP002115582 page 1093, left-hand column, line 1 - line 22 ---	1
Y	EP 0 776 671 A (SIEMENS ELEMA AB) 4 June 1997 (1997-06-04) column 2, line 8 - line 41 ---	1
A	US 5 671 752 A (SINDERBY CHRISTER ET AL) 30 September 1997 (1997-09-30) column 10, line 15 - line 18; figure 1 --- -/--	1

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 September 1999	06/10/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Zeinstra, H

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 22377 A (UNIV MANITOBA ;YOUNES MAGDY (CA)) 26 June 1997 (1997-06-26) page 7, line 4 -page 9, line 28; figure 1	1
A	US 5 353 788 A (MILES LAUGHTON E) 11 October 1994 (1994-10-11)	
P,X	WO 98 48877 A (GRASSINO ALEJANDRO ;SINDERBY CHRISTER (SE); FRIBERG SVEN (SE); LIN) 5 November 1998 (1998-11-05) page 10, line 22 -page 11, line 4; figures 1-5 page 16, line 14 -page 17, line 19 page 19, line 16 -page 22, line 4; figure 10	1

INTERNATIONAL SEARCH REPORT

nformation on patent family members

Inter tional Application No
PC /CA 99/00529

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0776671 A	04-06-1997	JP 9173454 A	08-07-1997
		US 5720278 A	24-02-1998
US 5671752 A	30-09-1997	CA 2172329 A	01-10-1996
		US 5820560 A	13-10-1998
WO 9722377 A	26-06-1997	AU 1090897 A	14-07-1997
		CA 2240733 A	26-06-1997
		EP 0871509 A	21-10-1998
		JP 11502755 T	09-03-1999
US 5353788 A	11-10-1994	NONE	
WO 9848877 A	05-11-1998	US 5820560 A	13-10-1998
		AU 3534497 A	24-11-1998

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
GP/10875.79		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 99/ 00529	04/06/1999	04/06/1998
Applicant		
UNIVERSIT DE MONTR AL et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   PROPORTIONNAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 10

   [X] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 99/00529

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M16/00 A61B5/0488

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols).
IPC 6 A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	E. AGOSTINI ET AL.: "Electromyography of the diaphragm in man and transdiaphragmatic pressure" JOURNAL OF APPLIED PHYSIOLOGY, vol. 15, 1960, pages 1093-1097, XP002115582 page 1093, left-hand column, line 1 - line 22 ---	1
Y	EP 0 776 671 A (SIEMENS ELEMA AB) 4 June 1997 (1997-06-04) column 2, line 8 - line 41 ---	1
A	US 5 671 752 A (SINDERBY CHRISTER ET AL) 30 September 1997 (1997-09-30) column 10, line 15 - line 18; figure 1 ---	1
	-/--	

[X] Further documents are listed in the continuation of box C.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 22377 A (UNIV MANITOBA ;YOUNES MAGDY (CA)) 26 June 1997 (1997-06-26) page 7, line 4 -page 9, line 28; figure 1	1
A	US 5 353 788 A (MILES LAUGHTON E) 11 October 1994 (1994-10-11)	
P,X	WO 98 48877 A (GRASSINO ALEJANDRO ;SINDERBY CHRISTER (SE); FRIBERG SVEN (SE); LIN) 5 November 1998 (1998-11-05) page 10, line 22 -page 11, line 4; figures 1-5 page 16, line 14 -page 17, line 19 page 19, line 16 -page 22, line 4; figure 10	1

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INTERNATIONAL SEARCH REPORT

[redacted]mation on patent family members

[redacted]ternational Application No
[redacted]CT/CA 99/00529

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0776671 A	04-06-1997	JP 9173454 A	08-07-1997
		US 5720278 A	24-02-1998
US 5671752 A	30-09-1997	CA 2172329 A	01-10-1996
		US 5820560 A	13-10-1998
WO 9722377 A	26-06-1997	AU 1090897 A	14-07-1997
		CA 2240733 A	26-06-1997
		EP 0871509 A	21-10-1998
		JP 11502755 T	09-03-1999
US 5353788 A	11-10-1994	NONE	
WO 9848877 A	05-11-1998	US 5820560 A	13-10-1998
		AU 3534497 A	24-11-1998